V. *On Cerebral Anæmia and the Effects which follow Ligation of the Cerebral Arteries.*

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SECTION I.—*General Historical Review.*

THE opinions of early writers, which are on this subject both curious and interesting, are stated by MORGAGNI,* and criticised, or rather ridiculed, in BELL'S 'Anatomy.'† An analysis of the literature up to 1845 is given by NORMAN CHEVERS,‡ and up to 1860 by EHRMANN.§ Exact and important experiments date from those performed by MAYER in 1833. The experimental results obtained are, in abstract, as follows :—

1. MAYER : || *Horse.*—Both carotids ligatured.

Results.—Restlessness, gaping, drooping of the eyelids, increased restlessness, staggering. In $2\frac{1}{2}$ hours eyes and ears insensitive to touch, respiration less frequent, swooning, convulsions. In 2 hours 50 minutes spasm of respiration, tetanic convulsions, failure of respiration, death. In the horse the vertebral arteries, at their entrance into the skull, are comparatively of insignificant size.

Goat.—Two carotids tied and one subclavian, the latter peripherally to the vertebral artery.

* 'Epist. Anat. Med. 19,' art. 22, p. 153, in "De Sedibus et Causis Morborum," Patavi, 1765.

† Vol. 2, p. 88.

‡ 'Lond. Med. Gaz.,' vol. 36, p. 1140, 1845.

§ 'Des effets sur l'encéphale par l'oblitération des vaisseaux artériels,' Paris, 1860.

|| 'Act. Phys. Med. Acad. Caes. Leopold. Carol.' Bonn, 1833, vol. 16, p. 2.

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Result.—The pulse frequency in $3\frac{1}{2}$ hours decreased from 200 to 82, the respiration from 32 to 24. Hyper-sensitiveness contractions of the hind limbs, eyes closed, head and ears hung downwards. By 7th hour the head touched the ground, the eye and ears were insensitive. At 15th hour, restlessness alternating with sleep, circus movement to left. Swooning, convulsions at 18th hour. On third day, inability to stand. Renewed convulsions and death on the fourth day.

Goat and Ram.—Injection of wax into peripheral end of carotid, embolism of all cerebral arteries including basilar.

Results.—Immediate swooning, failure of respiration, slight convulsions, death.

Rabbit.—Embolism of cerebral arteries produced by injection of mercury.

Results.—Convulsions, followed by failure of respiration within 3 minutes.

Rabbit.—Ligation of the left subclavian and innominate arteries.

Results.—Immediate paralysis of muscles of neck and fore-limbs, dilation of pupils, tetanic convulsions, death.

Rabbit.—Ligation of both carotids.

Results.—As a rule nil. In one rabbit there followed hyper-reflex excitability, shivering, unequal pupils, drooping of eyelids, eyes and ears alternately sensitive and insensitive to touch, circus movements. In the 9th hour convulsions and death.

Pigeon.—Ligation of both carotid and both pectoral arteries.

Results.—Immediate convulsions and death.

Pigeon.—Ligation of both carotids.

Results.—Weakness of sight, trembling and inability to stand, infrequent respiration, convulsions and death on the fourth day.

2. JOBERT DE LAMBALLE: *Horse.*—According to N. CHEVERS the two carotids were ligatured in a horse by JOBERT DE LAMBALLE, and there resulted convulsions and death.

3. ALESSANDRI:* *Horse.*—Ligation of the carotids, an interval of thirty-six days between the application of the first and second ligature.

Results.—The horse fell to one side when the second artery was tied, but quickly recovered.

4. ASTLEY COOPER:† *Rabbit.*—Both carotids tied, and then compression of the vertebral arteries.

Results.—Convulsions, failure of respiration. On discontinuing the compression, the rabbit drew a spasmodic breath and revived. It then lay on its side, making convulsive movements and breathing spasmodically. Recovered by second hour.

Dog.—Ligation of both carotids and both vertebrals. The latter at their origin from the subclavian.

Results.—Immediate loss of sensibility and staggering as if intoxicated, dilated pupils, swooning, convulsions. Stupor and paresis followed. On the third day

* 'Schmidt's Jahrbücher,' vol. 26, p. 322, 1840.

† 'Guy's Hospital Reports,' vol. 1, p. 465, 1836.

recovery was complete, and the animal lived as a good house dog for nine months. The anastomotic arteries, developed in this dog, are preserved in the museum of the Royal College of Surgeons.

5. PANUM :* *Dog.*—Repetition of A. COOPER's experiment, but ligation of the vertebrals at the level of the axis vertebra. PANUM is in error in supposing that COOPER tied the arteries at this spot.

6. KUSSMAUL and TENNER :† *Rabbits.*—Occlusion of the carotid and subclavian arteries.

Results.—Contraction of sphincters, viz., iris, palpebral fissure, mouth, nose, retraction of eyeballs. Respiration accelerated, later prolonged and deepened. Dilatation of sphincters, eyeballs prominent, converged and then rolled towards external angles of their sockets. Swooning, general convulsions in 8—18 seconds.

Order of convulsions—tonic spasm of neck-muscles, retraction of head, dilatation of pupils, trismus. Animal next flung itself forwards with great force. There followed clonic flexor and extensor movements of the limbs, and fixation of the eyeballs with the pupil in the centre of the palpebral fissures. The respiration became shallow, while the pulse remained vigorous. The clonus was replaced by tonus, and this by paralysis and flaccidity. The whole attack lasted 18—120 minutes, and was sometimes followed by a second but more tetanic fit accompanied by emission of fæces and urine. The fits immediately ceased, and the animals recovered on loosening the ligatures. The same convulsions were produced by ligation of the trachea or by bleeding. In one animal the thoracic aorta was clamped for 1 minute, and then the cerebral arteries compressed. In this case a head fit alone resulted, for the spinal centres had become paralysed by anæmia.

After division of the neural axis above the pons, convulsions could be evoked by compressing the cerebral arteries, while each renewal of the blood stream, for a time, inhibited the opisthotonos produced by the lesion. Extensor rigidity, produced by ablation of the cerebellum, was abolished by compression of the cerebral arteries and convulsions in one case ensued. Convulsions failed to appear in debilitated or etherised rabbits, or when the cerebral anæmia was gradually produced.‡ KUSSMAUL and TENNER localised "a convulsive centre" in the spinal bulb.

They sealed a glass window into the skull (method of DONDERS) and observed that the pial vessels contracted when the cerebral arteries were compressed.§ The brain, however, did not collapse. During the convulsions the pial veins became swollen. When the cranium was opened the brain collapsed, to the extent of $2\frac{1}{2}$ millims., when the arteries were occluded, while during the convulsions the brain bulged into the opening. The convulsions were produced equally whether the cranium were

* 'Cannstadt's Jahresb.,' vol. 3, p. 239, 1859.

† 'Moleschott's Untersuch.,' vol. 3, p. 1, 1857.

‡ Confirmed by MAYER, 'Zeitsch. f. Heilk.,' vol. 4, p. 29, 1883.

§ Confirmed by EHRMANN, *loc. cit.*

closed or open, for it was the cessation of the circulation and not, as BURROWS supposed, the alteration in intra-cranial pressure that evoked the fit.*

KUSSMAUL and TENNER produced spasms in one rabbit by excitation of the cervical sympathetic after occluding three of the cerebral arteries. This result they attributed to vaso-motor constriction of the pial arteries. The experiment has not been confirmed by NOTHNAGEL and RIEGEL and JOLLY. GAERTNER and WAGNER, ROY and SHERRINGTON, BAYLISS and L. HILL have likewise been unable to find positive evidence of a cerebral vaso-motor supply in the cervical sympathetic nerves.† The convulsions were probably evoked by the spread of the excitation to the afferent fibres of the vagus.

7. ROSENTHAL‡ and MAYER:§ These authors questioned the conclusion of KUSSMAUL and TENNER that the anæmic convulsions are similar to those of epilepsy in its complete form. The convulsions exactly simulate those produced by asphyxia.

8. HERMANN and ESCHER:|| *Rabbits.*—Compression of the superior venæ cavæ and azygos veins.

Results.—No convulsions. The convulsions were obtained on subsequently blocking the vertebral sinuses.

9. FERRARI:¶ *Dogs.*—Embolism of the cranial sinuses by injection of wax.

Results.—Convulsions when every venous sinus was blocked. Recovery without symptoms when the anastomoses through the ophthalmic veins and vertebral sinuses were alone not embolised.

10. COUTY:** Embolism of all the cerebral arteries produced by injection of lycopodium spores in curarised animals.

Results.—Arrest of respiration, inhibition of the heart, vaso-constriction, and enormous rise of arterial pressure. Next acceleration of the heart, fall of arterial pressure, death. COUTY confirmed A. COOPER'S experiment. Dogs survive ligation of the four cerebral arteries.

11. BASTGEN:†† Embolism of the cerebral arteries produced by injection of oil.

Results.—Similar to those of COUTY.

12. MARKWALD:‡‡ Embolism of cerebral arteries produced by injection of wax. (*a*) Embolism of cerebrum.

Results.—Sopor, inability to walk, auditory and visual anæsthesia, loss of the

* JOLLY confirmed this conclusion by washing out the blood with normal saline, injected at arterial pressure ('Untersuch. u. d. Gehirndruck,' Wurzburg, 1871).

† *Cf.* LEONARD HILL, 'The Physiol. and Pathol. of the Cerebral Circulation,' p. 45, London, 1896.

‡ 'Arch. f. Physiol.,' 1865, p. 191, Berlin.

§ 'Zeitsch. f. Heilk.,' vol. 4, 1883.

|| 'Arch. f. d. g. Physiol.,' vol. 3, p. 3, 1870.

¶ 'Wien. Med. Jahrb.,' p. 81, 1888.

** 'Arch. de Physiol.,' p. 665, Paris, 1876.

†† 'Pulsfrequenz u. Hirndruck,' Dissert., Wurzburg, 1879.

‡‡ 'Zeitschr. f. Biol.,' vol. 26, p. 259, München, 1890.

sensibility of the position of the limbs. (*b*) Embolism of cerebrum and mid-brain. *Additional Results.*—Opisthotonos, tetanic spasms, loss of pupil and lid reflexes. If the vagi were divided, there followed inco-ordinate respiratory spasms of the diaphragm. (*c*) Embolism of basilar artery. *Results.*—Acceleration and then paralysis of respiration, rise and then fall of arterial pressure, general spasms, death.

The Ligation or Obliteration of the Cerebral Arteries in Man.

1. Norman Chevers* in 1845 analysed the literature on this subject. In twelve cases paralysis of the opposite side of the body occurred within eight days after ligation of one carotid artery. "Drowsiness, giddiness, delirium, and severe pain in the head" were common symptoms. In some cases unilateral or general convulsions.

2. Todd :† A dissecting aneurism suddenly obliterated the right common carotid artery.

Results.—Syncope, snoring-respiration, pupils rigid to light, the right pupil more dilated than the left. Subsequently mental inertia, paralysis of left side, and twitching of left arm.

3. John Davy :‡ A case of gradual obliteration by an aneurism of the subclavian, vertebral, and the left carotid arteries.

Results.—Temporary attacks of syncope and vertigo. Recovery. Anastomosis set up by way of the intercostal arteries.

4. Marshall Hall§ in the days of vampyrism noticed that patients when raised to the erect posture became convulsed after extensive bleeding. This was due to cerebral anæmia brought about by the determination of the blood to the lower parts.

5. Schiff|| twice compressed one of his own common carotids, and produced unilateral convulsions preceded by numbness and formication.

6. Kussmaul and Tenner :¶ Compression of both carotid arteries in six male adults. *Results*—paling of face, convulsive efforts to close eyelids, pupils first contracted, then dilated. Respiration slow, deep, and sighing. Next dizziness, staggering, swooning. In two cases general convulsions followed the maintenance of the compression. The spasms commenced with clonus of the face muscles. On ceasing the compression there occurred a deep-drawn breath, the pupils dilated still more, consciousness and voluntary power returned in a few seconds.

* *Loc. cit.*
† 'Med. Chir. Trans.,' vol. 27, p. 301, London, 1844.
‡ 'Res. Path. and Anat.,' vol. 1, p. 426, London, 1839.
§ 'On Blood-letting,' pp. 14 and 159, London, 1836.
|| 'Lehrb. d. Physiol.,' 1858–59, p. 108.
¶ *Loc. cit.*

"The epileptic convulsions," say KUSSMAUL and TENNER, "only manifest themselves in a man when, together with the cerebrum, some or all parts of the neural axis lying behind the optic thalami are suddenly deprived of blood; unconsciousness and insensibility originate in causes proceeding from the brain proper." Writing in 1859 these authors were unaware of cortical excitability or Jacksonian epilepsy.

7. EHRMANN* analysed forty-nine recorded cases of ligation of the common carotid artery. The most common symptoms were stupor, hemiplegia on the contra-lateral side, and dimness of vision on the same side. Unilateral convulsions occurred in some cases. Coma and death not infrequently resulted.

8. HORSLEY and SPENCER† analysed eighteen cases of ligation of the common carotid, in all of which more or less paralysis ensued. If the left carotid were tied, aphonia accompanied the paralysis. Convulsions were the exception, but this is to be expected when anæsthetics are employed. From ligation of both carotids (within 15 minutes), there resulted coma and death.‡ The two carotids have been in several cases, and successfully, tied when intervals of time (*e.g.*, $4\frac{1}{2}$ days) were allowed.§

ALEXANDER and others have proved that both vertebrals may be tied, and with but little risk. This operation, introduced for the relief of epilepsy, is not favoured by BINZWANGER.||

Summary of Section I.—Ligation in one operation of the four cerebral arteries is followed by convulsions and death in rabbits (MAYER, KUSSMAUL); by temporary paralysis and slight convulsions and recovery in dogs (A. COOPER, COUTY). Ligation of the two carotids produces convulsions and death in pigeons, goats, and horses, coma and death in man, while in most rabbits and in dogs the effect of this operation is nil. In all animals ligation of one carotid is followed by no symptoms, but in man hemiplegia and convulsions, and even coma and death, have not infrequently followed.

EXPERIMENTAL WORK.

The researches here described have been carried on from 1895 to 1900.

SECTION I.—*The Effect of Acute Cerebral Anæmia on the Bulbar Centres of Anæsthetised Animals.*

I have already published the records of this inquiry.¶

* *Loc. cit.*, p. 35.
† 'Brit. Med. Journ.,' 1889, vol. 1, p. 457.
‡ 'MOTT, Med. Phys. Journ.,' New York, vol. 7, p. 401, 1847.
§ 'EHRMANN,' *loc. cit.*, p. 21.
|| 'Die Epilepsie,' 1899, p. 413.
¶ 'The Cerebral Circulation,' p. 125, London, 1896.

Summary of Conclusions.

The results are the same, whether the blood-flow through the brain is stopped by ligation or embolism of all the cerebral arteries, or by compression of the cerebral vessels* brought about by the introduction of a foreign body within the cranial cavity. When the spinal bulb is suddenly rendered anæmic in the anæsthetised mammal, there results vaso-motor spasm, producing a very high aortic pressure, respiratory spasm, and spasm of the vagal centre, producing slowing or even arrest of the heart. The respiration is at first accelerated and deepened, there then follow deep inspiratory spasms of the diaphragm, accompanied by head-dyspnœa and separated by long pauses. The state of excitation of the bulbar centres is quickly followed by paralysis, as is shown by the fall of arterial pressure, the quickening of the pulse, and the cessation of respiration. Failure of the respiratory centre is in most cases the primary cause of death. This can be compensated for by artificial respiration.† In some cases vaso-motor paralysis precedes the failure of respiration. If three of the cerebral arteries be tied, then a marked rise of arterial pressure follows each compression, while on loosening this artery the effect is depressor.

Traube-Hering curves almost always occur when the spinal bulb is rendered severely but not completely anæmic, while Cheyne-Stokes respiration and rhythmic alterations of pulse frequency‡ sometimes ensue. The excitatory stage of spasm entirely fails in exhausted or over-anæsthetised animals. Ligation in one operation of both carotid and both vertebral arteries is almost immediately fatal in nearly but not quite all rabbits, and is fatal either at once or after the lapse of a few hours in all cats and monkeys.§ In dogs, on the other hand, the quadruple ligature hardly ever is followed by a fatal result. The difference depends on the fact that in dogs each superior intercostal artery sends a large branch which runs in with the brachial plexus, and enters the anterior spinal artery. These arteries after ligation of the other four dilate up to the size of the vertebrals, and supply the base of the brain with sufficient blood. On injecting dogs with carmine-gelatine after ligation of the four arteries, the base of the brain is found well injected, while only the larger arteries on the convex surface of the cerebrum are filled. A pressure was employed for injection equal to the arterial pressure, and in other parts of the body, such as the intestine, the vessels were completely filled. The cortex cerebri collapses, and becomes bloodless when the cranium is opened, and the cerebral arteries are compressed. There is no collapse when the hole in the cranium is closed by a glass window; nevertheless, the pial vessels constrict and the cortex pales. This is brought about

* *Cf.* HORSLEY and SPENCER, 'Phil. Trans.,' B, 1892.

† Recently a man in the London Hospital, with a large intraventricular cerebral hæmorrhage, was maintained alive for more than 10 hours by rhythmic excitation of the diaphragm.

‡ *Cf.* G. MAYER, 'Zeitsch. f. Heilk.,' vol. 4, p. 192, 1883.

§ I have, since 1896, determined that these animals all eventually die after a few hours, and thus must here modify the statement in my book.

in my opinion by a compensatory expansion of the veins at the base of the brain, for on cessation of the arterial flow the blood will, owing to the influence of gravity, congest to the lower parts of the brain. The amount of cerebro-spinal fluid is increased in dogs after the cerebral arteries have been tied for some hours.

I have recently had the opportunity, by the kindness of Mr. G. L. CHEATLE, of watching the effect of ligation of the right common carotid in man under the condition of chloroform anæsthesia. The arterial pressure was observed by means of the Hill-Barnard sphygmometer. The arterial pressure rose when the artery was tied from 110 to 140 millims. Hg, and the respiration became deeper and accelerated. In 5 minutes these changes were over, but the left pupil was more dilated while the right reacted less quickly to light. The operation was undertaken for the relief of aneurism. The arteries were degenerated and brittle, and the man died during the following day without recovering consciousness.

SECTION II.—*Cerebral Anæmia produced by Fixation in the Vertical Head-up Position.*

A. REGNARD* trephined the skull of two rabbits and suspended the animals in the vertical posture, with the head up. The brain became anæmic and collapsed, and in less than two minutes convulsions supervened and the animals died.

SALATHɆ proved that this rapid death only takes place when the rabbits have lost a great deal of blood, a fact which had previously been determined by MARSHALL HALL on dogs. SALATHÉ, nevertheless, found that suspension, with the head up, proved fatal to rabbits in 2½ hours at the latest. Six hours' suspension with the head down had no effect, for the animals when liberated ran about and ate at once. SALATHÉ mentions the case of a steeplejack who fell, caught his feet, and was suspended head downwards from the cross of a church for three hours. There occurred in this man no ill-effects. SALATHÉ placed the abdomen and legs of a rabbit in an air-chamber and lowered the pressure therein ; the blood was thus determined to these parts, and the animal died of convulsions in a few minutes. He also centrifugalised‡ dogs and rabbits. When the feet were directed outwards the rabbits died in 6—15 minutes, and dogs in 10—25 minutes. When the head was placed outwards death took place after a period more than twice as long.

I myself have shown that, after a preliminary section of the upper dorsal spinal cord has been made, and paralysis of the vaso-motor tone and abdominal muscles established, then the suspension of dogs in the erect posture often causes the whole of the blood to collect in the dilated abdominal vessels, the heart to empty, and the cerebral circulation to cease.§ The same thing occurs after bleeding (MARSHALL HALL).

* 'Congestion Cérébrale,' p. 26, Paris, 1868.

† 'Trav. du Lab. Marey,' 1877, p. 255.

‡ *Loc. cit.*, p. 267.

§ 'Journ. of Physiol.,' vol. 18, p. 15, 1895, and vol. 21, p. 323, 1897.

The cerebral circulation, although greatly diminished, is not entirely stopped by these means in cats and monkeys (and some dogs), for in these animals the abdominal blood-vessels and those of the hind limbs are sufficiently supported and confined by the taut abdominal wall and skin, even though the muscles have lost their tone. In other words, *animals with a tight drum-like abdominal wall are protected from the effects of suspension, while those with a loose abdominal wall are in danger of syncope.* This fact I have clearly demonstrated on rabbits by the following experiments* :—

I. *Strong Grey Hutch Rabbit.*

2.15 P.M. Suspended by the ears and fore feet, head upwards. The hind legs were fixed in the extended position.

2.20. Strong convulsive movements. Flexor and extensor spasms of the hind limbs.

2.25. Deep and prolonged respiration. Pupils dilated, rigid to light. Conjunctival reflex present. Repeated general convulsions.

2.34. Conjunctival reflex absent. Convulsive twitches of the legs continue. Shallow respiration.

2.35. Respiration ceased. The animal is placed horizontally, and artificial respiration begun.

2.36. Conjunctival reflex present ; breathing recommences.

2.53. Pupil still rigid to light. The animal sits in a condition of sopor.

3.5. The animal is running about.

3.10. Tends to walk on the back of the fore-paws. Completely recovered.

II. *Black Hutch Rabbit.*

11.0 A.M. Suspended head upwards.

11.7. Convulsions. The pupils dilated and rigid to light. Conjunctival reflex present.

11.15. Renewed convulsion. Pupils much more dilated. Lid reflex absent, but the membrana nictitans still closes on touching the cornea.

11.20. Convulsions, nystagmus, *typical Cheyne-Stokes respiration with a convulsion of the body at the height of each group.*

11.24. Respiratory gasps, head-dyspnœa, lips very anæmic.

11.25. Animal moribund. The abdomen was then bandaged with an elastic bandage. The respiration almost immediately returned.

11.27. The respiration is normal, and the lid reflex present. The pupils are still rigid to light.

* Prelim. Note, 'Physiol. Soc. Proc.,' March 12, 1898.

11.33 A.M. Pupils smaller and react sluggishly. The animal voluntarily moves its head.

11.35. Set free; the animal runs about the room, but walks on the back of its fore paws.

2.0. Perfectly normal.

III. *Two Black Hutch Rabbits,* A *and* B.

12.0 A.M. Both were suspended in the erect posture with the head up. The abdomen of one (B) was previously bandaged with a rubber bandage.

12.15 P.M. A is moribund, with pupil and lid reflex absent, after the usual convulsions and respiratory gasps. Recovery was brought about by compressing the abdomen. On ceasing to compress, syncope again occurred. On finally placing the animal horizontal it recovered, but was dull and unalert for an hour afterwards, and the hind limbs slipped under it. Died in the night.

12.25. B unaffected. The bandage was removed.

12.45. The animal is moribund. The animal recovered when placed in the horizontal posture, after temporary sopor and paralysis, but died in the night.

IV. *Grey Hutch Rabbit,* A.

2.33 P.M. Suspended, head up.

2.37. Convulsions.

2.38. Convulsions; pupils rigid, dilated.

2.42. Convulsion; lid reflex absent. Lips quite white.

2.44. Respiratory gasps; death.

Grey Hutch Rabbit, B.

2.52 P.M. Suspended, head up; abdomen bandaged.

3.35. Eats corn out of my hand.

4.0. No symptoms; is set free, and runs about at once.

V. *Black Hutch Rabbit.*

2.57 P.M. Suspended, head downwards.

4.0. Quite unaffected; ran about on being set free, brisk and alert as ever.

VI. *Sandy Hutch Rabbit.*

3.0 P.M. Suspended, head upwards.

3.6. Convulsions started by a sudden noise. The animal is hyperæsthetic.

3.10. Lips very pale; lid and pupil reflex absent.

3.15. Convulsions. Deep respirations.

3.35 P.M. The animal is now maintaining a sufficient circulation by deep respirations and occasional struggling. By these means the venous blood in the abdomen is returned to the heart. The lid reflex is present.

4.0. The animal is still maintaining the circulation by means of the respiratory pump, and on being set free soon runs about.

These experiments show that most hutch rabbits, with large atonic abdomens, rapidly die from cerebral anæmia when fixed in the erect posture. Death is preceded by the Kussmaul-Tenner convulsions, and is due to respiratory failure. They also show that the anæmia is completely prevented by bandaging the abdomen, and, further, that the brain can rapidly and completely recover from anæmia after the pupil has been rigid to light for 10—20 minutes.

On opening the thorax in the suspended rabbits it became evident that the weight of the abdominal organs draws down the diaphragm and pulls taut the vena cava inferior. The return of blood to the right heart is thereby prevented. The animal by its convulsions presses on and squeezes the abdominal organs, and thus temporarily relieves the congestion of the blood in the abdomen. If the hind limbs be left free they are also drawn up so as to compress the abdomen. The Kussmaul-Tenner convulsions therefore favour the cerebral circulation. If hutch rabbits be deeply chloralised before suspension, then death takes place extremely rapidly, for no convulsions occur. Chloral abolishes cortical excitability (VARIGNY), (FRANCK and PITRES).*

Experiment VII.

Two deeply chloralised hutch rabbits.

2.0 P.M. Suspended with the head up. The respiration stopped immediately; there occurred no convulsions. The respiration started again so soon as the animals were placed horizontally. This was repeated several times.

Experiment VIII.

Chloralised hutch rabbit.

The carotid arterial pressure was recorded.

2.25 P.M. Suspended, with the head up. The arterial pressure gradually and continuously fell.

2.27—2.30. Convulsions; the brain was exposed, it slowly collapsed. On squeezing the abdomen the arterial pressure was raised, the brain expanded and reddened, and the respiration started again. The convulsions produced the same effects.

* FRANCK, 'Fonct. Motr. d. Cerveau,' Paris, 1887.

Hutch rabbits having tonic abdomens and *all wild rabbits* are immune for many hours to the effects of suspension, and so are dogs, cats, and monkeys. These animals, just as man, if fixed in the erect posture finally die, but only after many hours. In man, it is said, there occurs under like conditions intense œdema of the lower parts and great thirst. Death no doubt results from cerebral anæmia, as the blood slowly sinks into the dependent parts owing to the exhaustion of muscular tone and the immobility of the limbs.

Experiment IX.

11.55 A.M. Two wild rabbits suspended with their heads upwards.

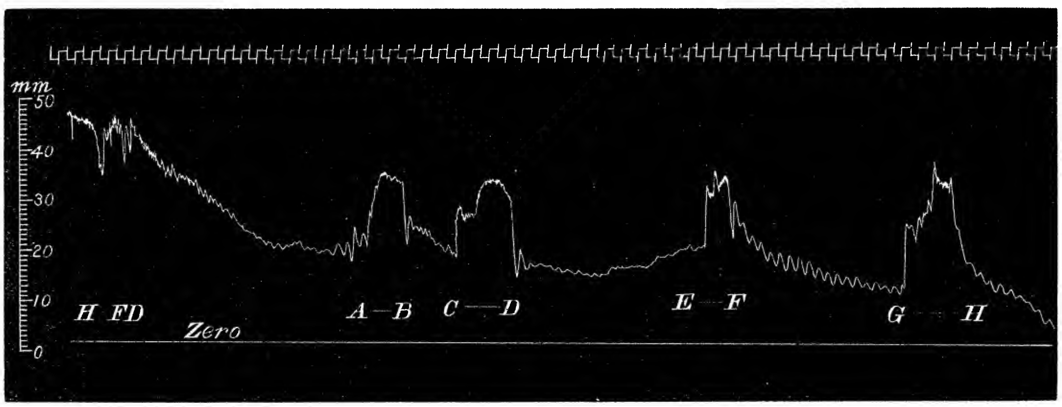
2.0 P.M. Set free ; there are no symptoms.

The circulation in the erect posture may fail in deeply chloralised wild rabbits just as in chloralised or deeply chloroformed dogs.

I have found* that the influence of gravity on the blood and viscera in the erect posture is balanced by sinking the rabbits in a bath of warm water. The hydrostatic pressure of the water outside balances, but not completely, that of the blood inside the body, while the water also causes the viscera to float upwards and so relieves the tension on the vena cava inferior.

Fig. 1.—Chloralised Hutch Rabbit.

Carotid pressure.



H. Horizontal. F, D. Immobilisation in the vertical feet-down posture. A. Immersed up to the heart in a bath of water at 47° C. B. Out of bath. C. In bath of concentrated salt solution. D. Out of bath. E. In bath of water at 48° C. F. Out of bath. G. In bath of water at 53° C. H. Out of bath. The high specific gravity of the salt bath makes no difference in the result. After the hot bath at 53° C. the fall is more rapid, owing to increased vaso-dilatation.

The effects of cerebral anæmia brought about by suspension are obviously the same as that brought about by ligation of the cerebral arteries, hæmorrhage, or electrocution, only the stages are more prolonged. For example, RICHET† after drawing

* Prelim. Note, 'Proc. of the Internat. Physiol. Congress' (1898), 'Journ. of Physiol.,' 1899.

† 'Dict. de Physiol.,' vol. 1, p. 497.

off a considerable quantity of blood, threw the heart of a dog into delirium by passing through it a powerful electric current. In 2 seconds there occurred rapid and deep respiration accompanied by vocalisation. By 18 seconds the latter became of maximal intensity and ceased at 30 seconds. The eye reflexes were at this stage preserved. At 40 seconds there occurred extensor spasms with intestinal contractions. The extensor spasms ceased together with the light reflex at 55 seconds, while the corneal reflex lasted to 1 minute 5 seconds.

Between 1 minute 25 seconds and 1 minute 50 seconds there occurred four long-drawn respiratory gasps, followed by paralysis of the respiratory centre.

S. MAYER states* that on renewing the circulation, the bulbar centres may recover in the rabbit after ligation of the four cerebral arteries has lasted for 10 minutes—that is to say, if artificial respiration be supplied during the period of ligation. The anæmia of the bulb is, however, under these conditions not absolute. CYON† interrupted an artificial circulation, which he had established through the brain, and found that the vaso-motor centre and the lid reflex might again be made active by renewing the blood supply after the lapse of 23 minutes. This was not the case with the respiratory centres. In my suspension experiments the bulbar centres are no doubt gradually exhausted both by the increasing anæmia and by the discharge of convulsions, and thus the respiratory centre, when it ceases to act, becomes irrevocably paralysed unless artificial respiration be at once applied.

In regard to the exhaustive effects of convulsions, ROTHMANN‡ states that the paralytic effects on the spinal cord of temporarily clamping the thoracic aorta are much severer if convulsive movements of the legs occur. SCHIFF§ had previously observed, in performing this same experiment, that paralysis follows immediately on convulsive movements, but does not occur for 10 minutes if the dogs remain quiet. The post-epileptic loss of cortical excitability is another and well-known example of the paralysing effect of convulsive discharges.

The lid reflex, depending on the fifth and seventh nerve nuclei, persists after removal of the cerebrum. My experiments show that the lid reflex vanishes but a short time before the failure of the respiratory centre, while the pupil reflex becomes lost considerably earlier. The closing reflex for the membrana nictitans, which is under the control of the cervical sympathetic, persists a little later than the lid reflex.

* 'Ctbltt. Med. Wiss.,' p. 133, 1880.

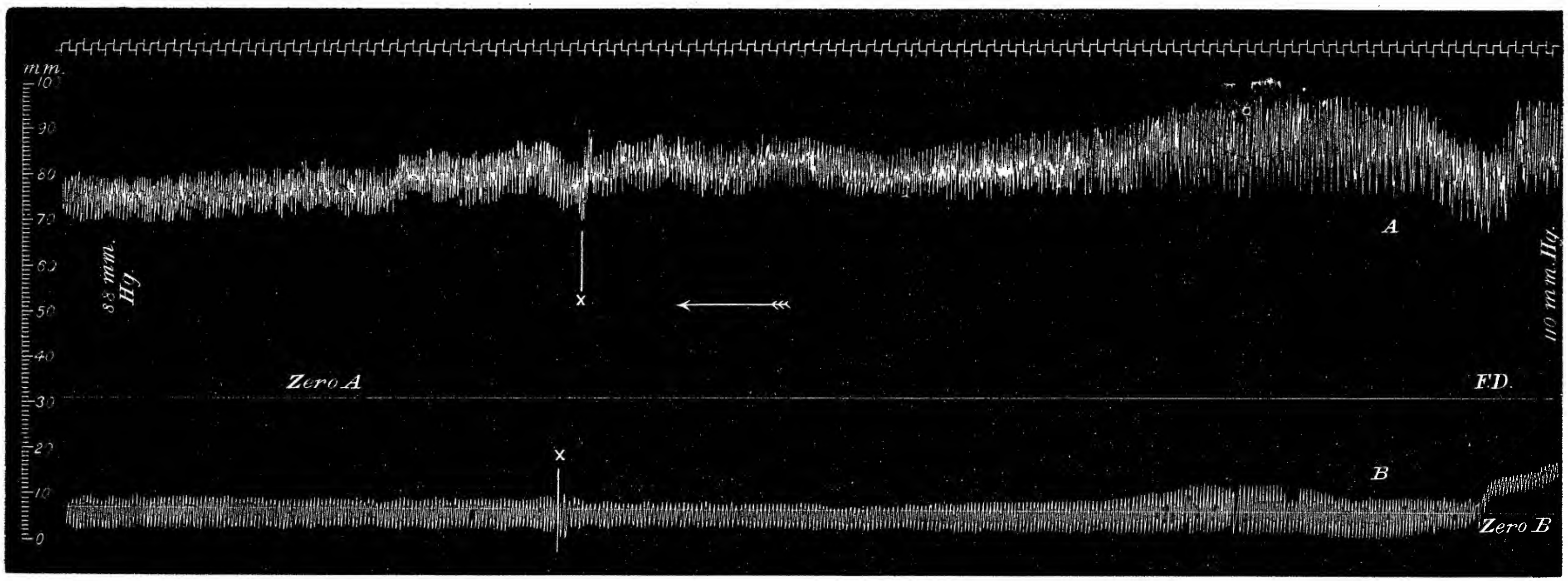
† 'Arch. f. d. g. Physiol.,' p. 254, 1899.

‡ 'Neurolog. Ctbltt.,' vol. 18, pp. 2 and 61, 1899.

§ 'Lehrb. d. Physiol.,' 1858–59, p. 102.

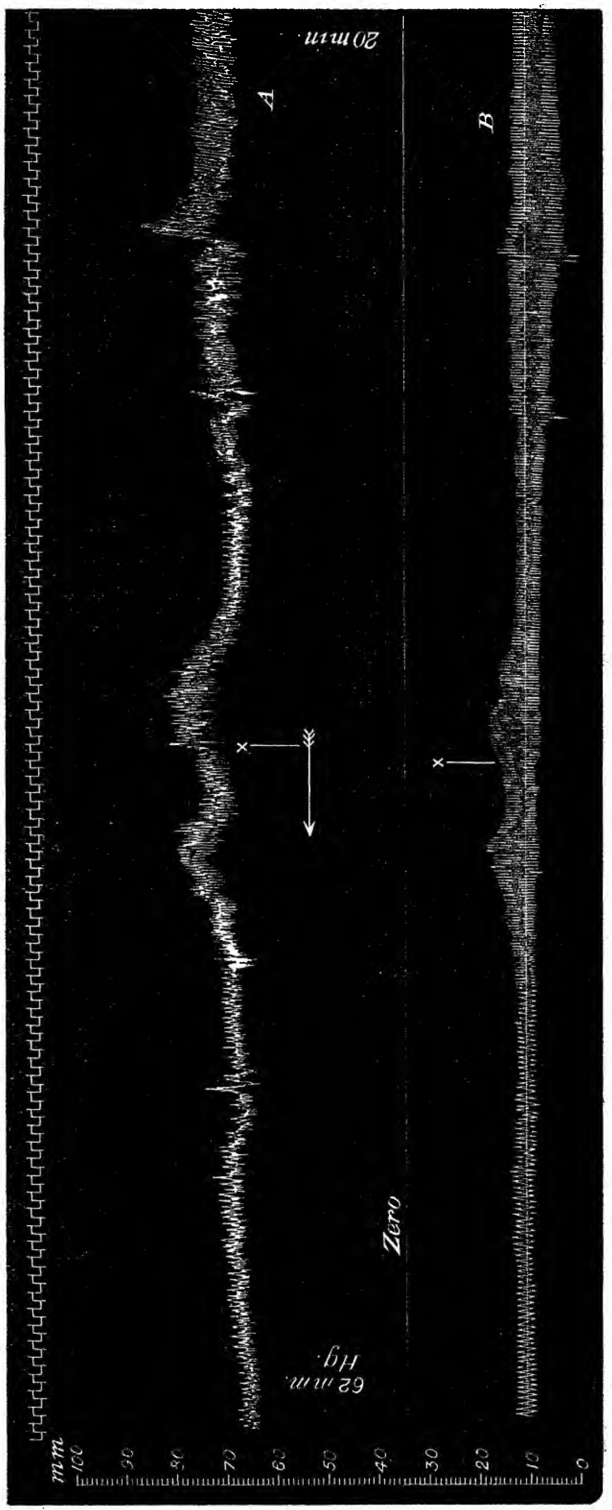
Fig. 2.—**Effect of Suspension with the Head up on a Dog (debilitated by a severe Catarrh of the Respiratory Tract and Conjunctivæ).**

Anæsthetic—Ether.



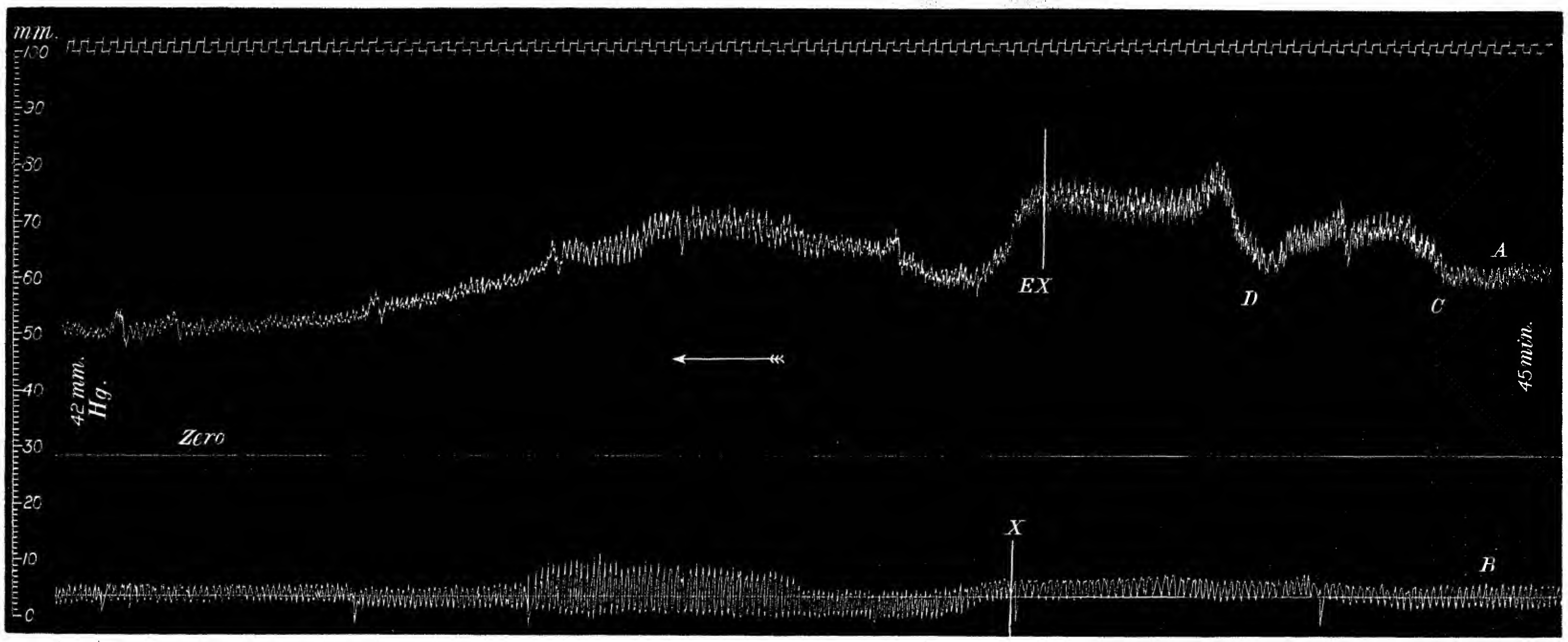
A. Carotid pressure. B. Vena cava superior pressure (recorded by Hg manometer). X. Corresponding points on the two tracings. Time tracing in 5″. F.D. Immobilised in the feet-down posture. Note fall of both pressures (the vena cava pressure from 10 to 0 millims. Hg), the increase of respiratory oscillations, followed by compensatory rise of arterial pressure. After 3 minutes the respiratory oscillations become less and the arterial pressure begins to fall slowly and steadily. Traube-Hering oscillations appear on both curves. At the end of this tracing the carotid pressure has fallen from 110 to 88 millims. Hg.

Fig. 3.—Same Experiment as Fig. 2, 20 minutes after Immobilisation.



Periods of increased respiration are seen now and again, by each of which the pressures are temporarily raised. By the end of this tracing the carotid pressure has fallen to 62 millims. Hg.

Fig. 4.—Same Expermient as Figs. 2 and 3, 45 minutes after Immobilisation.



Effect of immersing the dog in a bath of warm water up to the epigastrium. The vena cava pressure becomes positive and the arterial pressure rises. C. In bath. D. Level of water raised to epigastrium. E. Out of bath. At the end of this tracing the carotid pressure has fallen to 42 millims. Hg.

Conclusions.—1. Death from cerebral anæmia is rapidly brought about by the immobilisation in the erect posture of rabbits with patulous abdomens. The same result occurs in dogs, cats, monkeys, and in man, after great loss of blood, or after paralysis of both the blood vessels and wall of the abdomen has been induced by disease, prolonged exposure, shock, or such means as division of the spinal cord in the upper dorsal region.

2. The symptoms of cerebral anæmia so induced are (1) accelerating and deepening of respiration; (2) convulsions, consisting of general clonic flexions and extensions of the limbs and body and tetanic spasms; (3) steady fall of carotid arterial pressure and increasing anæmia of the head; (4) loss of pupil reflex; (5) gasping respirations at long intervals and head dyspnœa; (6) loss of lid reflex; (7) paralysis of respiration.

3. Recovery is brought about by compression of the abdomen, immersion in a bath, or the return to the horizontal position.

4. The animal may completely and rapidly recover after the pupil reflex has been lost for 10—20 minutes.

SECTION III.—*On the Excitability of the Cerebral Cortex after Ligation of the Cerebral Arteries.*

Historical Review.

A nerve-muscle preparation, when deprived of blood, becomes at first hyper-excitable and finally paralysed.* If a ligature be bound round the arm, so as to obstruct the circulation, there results hyper-æsthesia, as is evidenced, firstly, by peculiar and disagreeable sensations, and finally by intense pains, at the same time the muscles become hyper-excitable to electrical excitation.† Salted frogs (in which the blood has been replaced by saline) exhibit a period of exalted reflex excitability, which precedes the stage of paralysis and death. The immediate effects of a complete and sudden cessation of the blood-flow in the brain are convulsions, accelerated and deepened respiration, and vaso-motor spasm. The final effect is total paralysis and death.

Deoxygenation of the blood, as by asphyxia, provokes exactly the same sequence of events. These facts prove the apparent universality of the law that whenever a healthy neuro-muscular tissue is rendered anæmic, a stage of hyper-excitability of function precedes that of paralysis. It has, moreover, been determined that the onset of these two stages is markedly delayed by cooling of the tissues, and this is so both in mammals and in cold-blooded animals.

HUGHLINGS JACKSON since 1864 has drawn attention to the fact that convulsions occur from embolism of cortical arteries. He writes, in 1888,‡ as follows:—"Com-

* *Cf.* RICHET, 'Physiol. des muscles et des nerfs,' 1883, p. 609, and article "Anémie," RICHET'S 'Dict. de Physiol.,' vol. 1, p. 492, 1895.

† RICHET, 'Dict. Physiol.,' vol. 4, p. 401.

‡ 'Brit. Med. Journ.,' vol. 2, p. 116, 1888.

plete arrest of circulation in an arterio-cortical area would produce destruction of nervous elements; but some anastomosis might lead to a comparative restoration of circulation, otherwise to comparative stagnation—to a semi-stagnant patch. Such a condition is likely to cause destruction of cells in the central part of the arterial area, and is one favourable for over-nutrition of an inferior kind of those at its periphery."

The experiments of SCHIFF prove that unilateral convulsions can occasionally be experimentally discharged by compression of the carotid in man. I have several times confirmed on myself the fact that compression of one carotid may produce unilateral clonic spasms.* The spasms are preceded by a march of peculiar tingling and pricking sensations. These run down the opposite side of the body, and, starting in the hand, from thence proceed to the arm, and then to the leg. The clonic spasms are movements of flexion of the fore-arm, and these are accompanied by a feeling of alarm and vertigo.

The cortical discharge is entirely unaccompanied by consciousness. Consciousness of the clonus is aroused by the arm striking the arm of the chair on which it rests, and tactile sensations, rather than muscular and joint sensations, demand my attention. The experiment is by no means successful in all men. Its success depends, no doubt, partly on the freedom of anastomosis in the circle of WILLIS, but chiefly, I believe, on the instability of the cortical *cells*.

When the "motor area" is inflamed, mechanical excitation easily provokes a reaction,† while in man Jacksonian epilepsy, or contracture, may result. The Rindenreiz-contracture of H. MUNK is due to *irritative* lesion of the cortex and is not apparent when union takes place by first intention. This form of contracture is best seen in monkeys; in dogs epilepsy is the more usual result (HITZIG). The contracture shifts from one group of muscles to another, and is more evident on movement than during repose.

Epilepsy and hyper-excitability of the cortex likewise result during the period of inflammatory reaction which follows immediately after the cortex has been cooled by the ether spray. The excitability is lost during the period of refrigeration.‡ An exaggeration of cortical excitability is, says FRANÇOIS FRANCK,§ always to be observed after a *single* epileptic fit has been provoked by stimulation. Now one striking and obvious result on the cortex of an epileptic fit is venous congestion of the pial vessels. The muscular spasms increase the vena cava pressure and the pressure in the venous sinuses (L. HILL).‖ A continuance of the fits leads to post-epileptic exhaustion, and no reaction is then possible.

It seems clear that in the first stage of anæmia or inflammation, the excitability of

* Prelim. note, 'B. M. J.,' vol. 1, p. 962, 1894.

† LUCIANI. *Cf.* FR. FRANCK, 'Fonct. du Cerveau,' Paris, 1887.

‡ OPENCHOWSKY, 'C. R. Soc. Biol.,' Jan. 20, 1883.

§ 'Fonct. du Cerveau.'

‖ 'Phys. and Path. of the Cerebral Circulation,' 1896.

the cortex is exalted, and it is probable that venous congestion produces the same result. So TARCHANOFF* states that the head-down posture hastens the development of excitability in the cortex of the new born, and attributes this to hyperæmia, while in truth this very position produces venous congestion of the brain.

Coarse irritation of the cortex with an electrical current cannot be regarded as doing otherwise than altering the nutrition of the cortical cells in a downward direction, and yet the effect of prolonged subminimal excitation is a condition of increased excitability (DE VARIGNY†).

In regard to toxic agents, nearly all substances produce, first, exaltation, and then paralysis of cerebral functions. Alcohols and anæsthetics produce this result. Morphia‡ in certain doses may exaggerate both cortical and reflex excitability in dogs, although the animals are, on the sensory side, brought by this drug into the condition of decerebrate animals. The convulsants cicutin, strychnine, cocaine,§ picrotoxin, cinchonidin,‖ acid sodium phosphate, and absinthe in small doses produce convulsion, and in larger doses paralysis. The fact that anæsthetics stop the action of convulsants shows that convulsions arise from the first stage and anæsthesia or paralysis from the second stage of disordered cerebral metabolism. This is borne out by the fact that after a convulsant has been administered a far less quantity of the anæsthetic agent is required to produce anæsthesia. There is no need to multiply further examples of the fact that hyper-excitability is, as a rule, the first result of a downward alteration of the metabolism of the nerve centres. The higher function of the brain is not excitability (Actionscapacität), but resistance to impulsive action (Actionswiderstand), and it is the latter which is the first to fail when nutrition becomes disordered. To put it in other words, "Bahnung" then becomes easy, while "Hemmung" fails. It is then to be expected that a stage of hyper-excitability would be found to precede paralysis when the cortex is rendered anæmic. Nevertheless, the evidence on this point is most conflicting, as can be gathered from the following review :—

1. HITZIG¶ noticed that the excitability of the motor area vanished after loss of blood.

2. VULPIAN determined that the excitability vanishes within 1 minute after the cessation of the heart beat or on tying the pial arteries.

3. COUTY,** after ligation of the carotid and vertebral arteries in the dog, found the excitability augmented. Mere exposure of the cortex on one side produced in these conditions "contracture" on the opposite side.

* 'Gaz. Hebd. de Méd.,' Paris, 1878, p. 448.

† 'Ctbltt. Med.,' p. 26, 1885.

‡ BUBNOFF and HEIDENHAIN, 'Arch. f. d. ges. Physiol.,' vol 26, p. 162, 1881.

§ RICHET, 'Dict. Physiol.,' vol. 4, p. 408.

‖ ROVIGHI e SANTINI, 'Med. Ctbltt.,' p. 101, 1883.

¶ 'Untersuch. ü. d. Gehirn.,' Berlin, p. 19, 1874.

** 'Compt. Rend.,' vol. 88, p. 604, 1879.

4. MINKOWSKI* obtained exactly the opposite result both in dogs and rabbits. According to this author, any diminution in the cerebral blood supply produces lessened excitability. He states that, after exclusion of the four arteries in dogs, the excitability of the cortex vanishes, even though there is little sign of anæmia present, and that not only the grey but the white substance of the brain becomes inexcitable.

5. ORCHANSKY† bled morphinised animals from the femoral artery. When one-fifth of the total blood was withdrawn, the cortical excitability became augmented, and the reflex reaction of the animals to sensory stimuli was exalted. When two-fifths to three-fifths of the blood was withdrawn the excitability vanished and a condition of sopor ensued. At a period when the cortex had become inexcitable the animals were often observed to raise themselves up and attempt movements of progression. The transfusion of normal salt solution caused the collapsed brain of the bled animals to expand, and sometimes brought the cortical excitability back. More often the action of the medullary centres was alone renewed.

6. TARCHANOFF states that the excitability is lessened by loss of blood ; while

7. FRANÇOIS FRANCK‡ is of opinion that the cortical excitability is increased by moderate anæmia, and disappears after abundant hæmorrhage. The reflex excitability is in this latter stage increased. In the last stage of asphyxia FRANCK found that cortical epilepsy could not be produced.

8. RISIEN RUSSELL§ says asphyxia diminishes and then abolishes cortical excitability, while the knee jerks are at first increased.

9. ADUCCO|| determined that the excitability of the cortex in morphinised and atropinised dogs is augmented after closure of both carotids. (Coil 11 centims. before, 15—16 centims. after.)

10. HORSLEY and SPENCER¶ compressed the carotid in the monkey. No change was obvious either in the pulsation of the anterior or posterior cerebral arteries. On the other hand, the pulsation ceased to be visible in the middle cerebral artery, for this artery is in direct line with the axis of the carotid as it enters the circle of WILLIS.

The cortical centre chosen for observation was excitable with the coil at 11 centims. before compression, at 8 centims. during compression, and at 9 centims. after loosening the carotid. The observations recorded by these authors are on one monkey only.

* 'U. d. Aenderungen d. elekt. Erregbarkeit des Gehirns,' &c., Inaug. Dissert., Königsberg i. Pr., 1881, A. *cit.* after HERING.

† 'Arch. f. Physiol.,' pp. 297—309, Berlin, 1883.

‡ 'Fonctions Motrices du Cerveau,' pp. 249 and 350, Paris, 1887.

§ 'Brit. Med. Journ.,' vol. 1, p. 326, 1892.

|| 'Arch. Ital. de Biol.,' vol. 14, p. 136, 1891.

¶ 'Brit. Med. Journ.,' vol. 1, pp. 457—460, London, 1891.

11. H. E. HERING* having determined that reflex excitability—as evidenced by stimulation of a posterior root and its effect on respiration—was rapidly and completely abolished by ligation of the thoracic aorta, investigated the effect of ligation of the cerebral arteries. He writes: "Nach Abklemmung der letzten Hirnarterie trat, bei den verschiedenen Thieren mit verschiedener Geschwindigkeit, volkommene Unerregbarkeit nicht nur der Hirnrinde, sondern auch der weissen Marksubstanz ein. Nach Freigeben der Circulation kehrte die Erregbarkeit wieder zurück, nach Wiederabklemmung schwand sie wieder." HERING ligatured the carotids and subclavian arteries central to the origin of the vertebrals.

12. BROCA and SOURY† conclude that the cortical excitability of chloralised dogs is abolished by asphyxiation in 3 to 4 minutes. In artificially cooled animals the cerebral circulation can be arrested for many minutes without loss of cortical excitability, just as reflex excitability persists longer in an iced "salted" frog than in one kept at 30° C. Cortical excitability vanishes within 30 seconds after complete anæmia has been established by vagal arrest of the heart, or by ligation of the subclavian and carotid arteries. Reflex hyper-excitability is evident at the stage when the cortex cerebri has become inexcitable.

Summary of Historical Evidence.

There can be no doubt that complete anæmia of the brain abolishes cortical excitability in 1 minute. On the other hand, the evidence concerning the effect of partial anæmia is most conflicting. It is not possible to harmonise the observations of MINKOWSKI with those of COUTY and ORCHANSKY, nor those of ADUCCO with that of HORSLEY and SPENCER. It is clear that such divergent results may depend not only upon differences in technique, but on differences in individual animals. In such a case as this a positive result is of greater worth than a negative. The degree of anæmia produced by ligation of the four cerebral arteries is not the same in the dog as in the rabbit or monkey, and this fact has not been taken into account by previous writers. It is, moreover, no easy matter to satisfactorily investigate the cortical excitability in any other animal than the monkey. It is often a matter of no little difficulty to demonstrate cortical excitability in dogs, that is to say, when the dogs are etherised and the cortex exposed and at once excited. The same difficulty has been noted by HITZIG and others. BROWN SEQUARD‡ states that the exposed cortex of unnarcotised dogs and rabbits may often be quite inexcitable while the animals are running about the room in a normal manner. The movements of guinea-pigs are, on the other hand, rendered choreiform by mere exposure of the cortex, while, according to COUTY,§ monkeys become paresed after this operation. Resistance of the human

* 'Centralblatt f. Physiol.,' vol. 12, pp. 313—317, 1898.

† RICHET'S 'Dict. de Physiol.,' article "Cerveau."

‡ 'C. R. Soc. Biol.,' p. 354, 1888.

§ 'C. R. Soc. Biol.,' p. 355, note, 1888.

cortex to excitation has been recorded more than once.* In a case recorded by GOTCH the anæsthetic was diminished until the patient reacted to the prick of a pin. The strength of current employed was intolerable to the tongue. This lack of excitability cannot be altogether ascribed to the insulation of the motor cells by non-excitable association areas. The "Hemmung" processes are, I believe, more marked in some animals than in others, and vary with the condition of the cortex. If dogs be left quiet for an hour, after the completion of the operation, then the cortical reactions are far more uniformly obtained. A partial explanation of the confliction of evidence concerning the excitability of the anæmic dog's cortex may be found in this fact. Moreover some workers may by operative methods cause greater loss of blood and depression of the vaso-motor centre than others, and thus influence the results obtained on ligation of the cerebral arteries.

EXPERIMENTAL RESULTS.

By a large series of experiments on dogs and monkeys, I have come to the conclusion that partial anæmia sometimes diminishes and abolishes, but more often exalts, cortical excitability. The exaltation is more evident in young animals, and usually persists when four of the cerebral arteries have been tied in the dog and three in the monkey.

Since a dog may normally run about after its cortex has been exposed (BR. SEQUARD), while a monkey is paresed by this operation (COUTY), and the dog's cortex may be inexcitable, while the monkey's is always most excitable, it would appear, supposing the above observations to be correct, as if a certain decrease in the normal functions of the cortex favoured excitability. In support of this theory I have found that if the four cerebral arteries be tied before the cortex of the dog is exposed, then, in such case, the operation is bloodless, while the cortex is as a rule most excitable immediately after exposure. This result shows that the cortex is not paralysed by operative insults, but is rendered excitable by a diminution in the velocity of blood-flow. The increased excitability may be due either to a chemical change, *e.g.*, increase of CO_2† in the motor cells of the cortex, or to the fact that the power of *resistance to activity* (Hemmung) ceases owing to the blockage of association pathways and the sensory projection. The sensory stimulations normally stream into the cortex and there revive memories, which together with the present sensations now inhibit and now exalt each other and so control the discharge of the motor cells.

Method of Experiment.—The animals were anæsthetised with chloroform and ether and subsequently with ether alone. They were placed on a water-bed filled with warm water. The skull was trephined, and, if necessary, the hole was enlarged with

* *Cf.* HORSLEY, 'Phil. Trans.,' B, 1890.

† In this connection I may recall the exaltation of the current of action in nerve produced by CO_2 (WALLER).

forceps. Hæmorrhage from the bone was stopped with wax. The dura mater was picked up with a curved needle, carefully incised, and reflected to the limits of the opening. The cortex was protected with pads of wool soaked in warm normal saline solution. It was excited by the tetanising current of the Du Bois coil worked by a single Leclanché cell. Between each excitation the primary current was broken so as to maintain the constancy of the current. Needle electrodes were employed with points 1 millim. apart.

Experiments.

Dog I.

10.0 A.M. Cortex exposed over crucial sulcus and the post-crucial convulsion excited; no reaction obtained.

11.15. Extension and advancement of the opposite fore-paw was obtained with a strong current (just bearable to the tongue).

11.20. Both carotids and vertebrals exposed and ligatures placed in position.

11.25. Cortex excited with same strength of current; no reaction.

11.27. Both carotid and vertebral arteries ligatured. The pupils at first contracted and then dilated. Cortex excited with the same strength of current, extension of the arm immediately obtained, and this passed on into an epileptic fit. The cortex on ligation of the arteries had markedly paled and collapsed. The pial veins, which before were large and distended, now became flat and flabby, and blew in and out with each respiration.

1.0 P.M. The cortex remained excitable while the reflex reaction to sensory excitation had become much increased.

Dog II. A large Mongrel Terrier of Middle Age.

March 8.

1.0 P.M. Two carotid and two vertebral arteries tied.

3.0 P.M. Marked extensor rigidity of the fore-limbs and hyper-reflex excitability.

March 9.

10.0 A.M. Animal soporose. On arousing it to walk the front legs are held scissorwise and the hind legs straddle widely and slip under it. The movements are slowly executed and ataxic.

The animal can be put into the oddest positions, and falls into sopor in such positions. A photograph was taken of the animal propped up against a box and standing on its head. The animal takes no notice of an artery clip placed on the pad of the foot.

Aroused to walk it snuffs along with its head on the ground, and when called comes in the right direction. It turns its head away from a

lighted taper, but shows neither fear nor excitement either at the flame or a cat. It ignored the presence of a rabbit which was placed in its path.

11.0 A.M. The animal was anæsthetised and injected (subcutaneously) with a saturated solution of EHRLICH'S methylene blue in doses of 30 cub. centims. at intervals of one-quarter to half an hour.

3.30 P.M. 285 cub. centims. of methylene-blue had now been injected and the cortex was exposed. There was no hæmorrhage from the diploe; the pia exhibited huge veins and insignificant arterioles. The brain only showed respiratory oscillations, and was collapsed from the skull wall. The cortex was stained blue very faintly. On exciting the post-crucial convolution with a strength of current comfortable to the tongue, an immediate extension and advancement of the opposite fore-paw was obtained. On again exciting the cortex there resulted a fit, and the cortex seemed to pale. It was difficult to be sure of this as the blue coloration was exceeding slight. Chloroform was then pressed, and the cortex became inexcitable as the anæsthesia deepened. On placing the animal head downwards and in the vertical position, the veins of the pia became greatly swollen and the brain bulged into the skull opening.

Dog III.

This dog was kept for more than a fortnight, so that its habits became familiar.

December 20.

10.0 A.M. The four cerebral arteries ligatured under ether and chloroform.

3.0 P.M. The dog is wandering about aimlessly and restlessly. It does not recognise familiar objects or persons. It avoids obstacles and a lighted match.

December 21.

10.0 A.M. The dog is paretic; its feet tend to slide out on a smooth surface, and it cannot lift its leg to make water. It circuses continually to the left. The head, owing to the deficient circulation, is colder than the body. The dog comes to a call, and is less idiotic than yesterday.

The cortex is exposed; there is no hæmorrhage from the bone; the quantity of cerebro-spinal fluid is greater than normal; the veins in the pia are very large, and the small arteries insignificant.

The brain collapses after opening the dura.

On excitation of the post-crucial convolution with a strength of current comfortable to the tongue, advancement of the fore-limb and drawing up of the hind limb is obtained with great ease. The excitability disappears after a few inhalations of ether, and re-

appeared after a few breaths of pure air. After administering more ether extensor rigidity ensues, and the excitability becomes abolished. Ten minutes later the respiration fails.

Dog IV.

3.0 P.M. The four arteries are ligatured. Next day the symptoms are similar to those described in the last dog, but are less marked. On exposing the cortex, the conditions of the pial vessels are similar to those seen in the last dog, and the excitability of the cortex is as easily demonstrated. By injecting methylene blue into this animal extensor rigidity is produced, the cortical excitability at the same time disappears, and the respiration quickly fails.

Large Dog, V.

12.30 P.M. Two carotids ligatured, cortex exposed, and post-crucial convolution excited. Extension of fore-paw is obtained with a strength of current comfortable to the tongue.

12.50 P.M. Right subclavian ligatured, central to the vertebral and superior inter-costal arteries. The same strength of current produces a clonic fit of the whole fore-paw.

1.0 P.M. Left subclavian ligatured. The respiration at once becomes deepened and accelerated, the pulse slow and of high tension. The respiration quickly fails. There occurs great venous congestion of the cortex (owing to respiratory spasms), and the excitability vanishes. Artificial respiration is quickly established, and the circulation remains in excellent condition. The pial veins, near the longitudinal sinus, flap full on each inspiratory inblast, and collapse on each out-blast. These veins also flap with each heart beat. The blood in the venous sinuses is thus driven in and out of the pial veins. The cortex remains quite inexcitable.

Dog VI.

Witness, Professor V. HORSLEY.

10.50 A.M. 30 cub. centims. of sat. sol. methylene blue injected intravenously.

11.0 A.M. Four cerebral arteries ligatured. The animal was then injected subcutaneously with methylene blue.

3.30 P.M. 180 cub. centims. of methylene blue have now been injected. The dog exhibits slight extensor rigidity and hyper-reflex excitability. The cortex is exposed; the blue tint is distinctly visible. The fore-limb area is excited with a strength of current comfortable to the tongue.

A well-marked reaction leading to a slight fit results. The cortex pales strikingly. Fifteen minutes later the blue colour has returned, and the same experiment is repeated. When the cortex is excited and no motor reaction results, then, in such case, no paling of the blue colour occurs. At 5 P.M. the animal is killed. I am indebted to Professor V. HORSLEY, who witnessed this experiment, for the suggestion to test on anæmic brains EHRLICH'S important and interesting experiment with methylene blue. I have since repeated the experiment on two normal animals, and have found, as EHRLICH and HORSLEY, that the cortex pales on excitation when a movement results, but not otherwise.

Dog VII.

The four cerebral arteries were tied, and the excitability of the cortex demonstrated at a meeting of the Physiological Society. The reactions were of a convulsive character. There was marked hyper-reflex excitability when the anæsthesia was reduced in amount. In three experiments the results have been of an inconclusive or negative character. In each of these cases the cortex was exposed before the arteries were tied.

EXPERIMENTS ON MONKEYS.

I. *Cercopithecus Viridis.*

Witnesses, Dr. W. HUNTER and Major HASSAN.

Ligatures are loosely placed in position on the two carotids, the right subclavian and the left vertebral.

The cerebral cortex is exposed over the mid-Rolandic area on both sides. The brain bulges, is very vascular and pink in colour, with small veins. Ascending frontal convolution excited. Extension and rotation of the wrist, advancing of the arm, and grasping movement of the hand are obtained on both sides with a strength of current which is just distinctly sensible to the tongue. With a weaker current there is no response.

Right carotid tied. There is slight paling on the same side. The excitability is the same on both sides.

Five minutes later *left carotid tied.* The left side is now slightly the less vascular; both sides of the brain are collapsed. There is no difference in excitability. The same movements are obtained with the same strength of current.

Five minutes later *right subclavian tied.* The pial veins are now fuller, and the brain is very distinctly collapsed on both sides. The cortex is excited by the same strength of current as before, and the response is equally good. After a rest of 15 minutes the shoulder area is found to be very excitable. The response is more

immediate and marked than before. Movements of the hand are less easily obtained.

Left vertebral tied. The respiration immediately deepens. The brain appears completely anæmic, very pale and depressed ; the pial veins contain blood, but are not at all distended. The cortex is quite inexcitable, even to the strongest currents. The respiration becomes typical of bulbar anæmia—long convulsive gasps, with head dyspnœa, and the mouth widely gaping, followed by long pauses. Each gasp is preceded by several abortive twitches of the diaphragm. The pulse is strong and of high tension. The respiration is improved by the head-down posture. The animal dies half an hour later from gradual failure of respiration, the gasps taking place at longer and longer intervals. There occurred no extensor rigidity.

II. *Rhesus Monkey.*

Witnesses, Dr. W. Hunter and Major Hassan.

Cortex exposed on both sides over the mid-Rolandic area. Ascending parietal convolution excited. Flexion of the thumb and fingers, as in grasping, obtained on both sides by exciting with a minimal strength of current, *i.e.*, just perceptible to the tongue. The excitability is notably diminished by deepening the anæsthesia.

Left carotid tied. No perceptible difference in the appearance of the pial vessels. By stimulating behind and in front of the fissure of Rolando, the following movements are obtained, equally, on either side, and with the above strength of current: Conjugate deviation of eyes, movements of jaw, retraction of lip, grasping of finger and thumb with pronation of the wrist.

Ten minutes later *right carotid ligatured.* The anæmia and collapse of the brain are now marked on both sides. The excitability is unchanged.

Five minutes later *right subclavian artery tied.* The brain is still more collapsed. The excitability on either side is undiminished. After half an hour's rest there ensues marked reflex hyper-excitability. The animal convulsively lifts itself up on its four limbs on the slightest touch. The excitability of the cortex to the same strength of current is very good, if anything increased rather than diminished.

Left subclavian vein tied (by mistake for the artery, as verified afterwards). On now exciting the arm area fits are obtained, the whole arm passing into clonus. The heart is opened, and the excitability is found to vanish in the course of 1 minute.

III. *Rhesus Monkey.*

The cortex is exposed over the mid-Rolandic region, and stimulated behind the fissure of Rolando. Grasping movements of the thumb and fingers are excited on both sides with a strength of current *barely* perceptible to the tongue.

Right carotid tied. No difference perceptible either in pial circulation or in excitability.

Five minutes later *left carotid tied.* The brain becomes much flatter, and the pial veins enlarged. The respiratory oscillations are increased, and the cardiac oscillations diminished. The excitability is as good as ever.

Five minutes later *right subclavian vein tied.* The pial veins become in consequence less congested. The excitability is unaffected. *Five minims essential oil of absinthe injected intravenously.* A tonic extensor spasm results. There is no clonus. Respiratory spasms follow, and death.

IV. *Bonnet Monkey.*

Witness, Dr. F. MOTT.

Ligatures placed in position on right and left carotids, on right subclavian and left vertebral.

Cerebral cortex exposed over arm area on both sides. Coil at $6\frac{1}{2}$ centims., a weak current just perceptible to tongue. Excitation of ascending parietal convolution. Movements localised—left cortex, clenching and extension of right wrist; right cortex, extension and pronotion of left wrist. Right carotid ligatured. Perceptible shrinking of right cortex; very slight paling, respiratory oscillations of the brain increased; and cardiac oscillations diminished on this side.

Coil at $6\frac{1}{2}$ centims. Stimulation provokes the same movements as above in undiminished strength.

Left carotid ligatured. Respiration at once troubled. Both sides of the brain depressed, but the left more so. Pial veins full.

Coil at $6\frac{1}{2}$ centims. Stimulation of left cortex *immediately* provokes a fit on the right. Pupils dilate, the left larger, rigid to light. Head dyspnœa, alæ nasi working and gaping of mouth.

Three minutes later clonic spasms of left leg.

Coil $6\frac{1}{2}$ centims. Arm area very, and now equally, excitable on both sides.

10 minutes later. Extensor rigidity of arm and leg on right side, and slight rigidity of left arm.

10 ,, ,, Pupils now equal and rigid to light. Hyper-reflex excitability very marked. Animal heaves up its body on the slightest touch.

20 ,, ,, Anæsthetic pushed. Rigidity vanishes except in right arm.

25 ,, ,, Both cortices became inexcitable to coil at 4 centims.

26 ,, ,, Coil at 6·5. Clonus of left hand and fit of right arm obtained. Reflex hyper-excitability returning.

30 ,, ,, Five minims absinthe injected into femoral vein. Tonic spasm of left leg; left arm and left leg became rigid. Return of rigidity, and respiratory trouble marked. No clonus. Cortex now inexcitable.

32 minutes later. Five minims absinthe injected. Ineffectual spasms of diaphragm followed by head gaping and gasping respirations at long periods. Paralysis of respiration.

V. *Bonnet Monkey.*

The animal almost died from chloroform syncope. Ligatures are placed on the two carotid arteries and a cannula inserted in the jugular vein. The whole of the Rolandic area is exposed from top to bottom. The following movements are obtained with a current-strength just distinctly perceptible to the tongue.

Arm area. Pre-central convolution; abduction of wrist; pronation of wrist; advancement of arm, and grasping movements. Post-central convolution; flexion of thumb.

Leg area. Upper end of post-central convolution; drawing up of leg and movements of tail.

Face area. Lower part of central convolutions. Retraction of lip. Elevation of lip.

Conjugate deviation of the head and eyes is also obtained on stimulating the posterior part of mid-frontal convolution. On increasing the strength of current, an epileptic fit is obtained.

On ligaturing the two carotids, there results profound anæmia of the cortex, collapse of the brain, and cessation of the cerebral pulse.

Five minutes later the excitability is markedly diminished. The leg movements can be obtained easily, but the finer movements of the hand can no longer be provoked.

Fifteen minutes later the cortical excitability is abolished. The carotids are now loosened, the brain flushes, expands, and pulsates; the excitability rapidly returns.

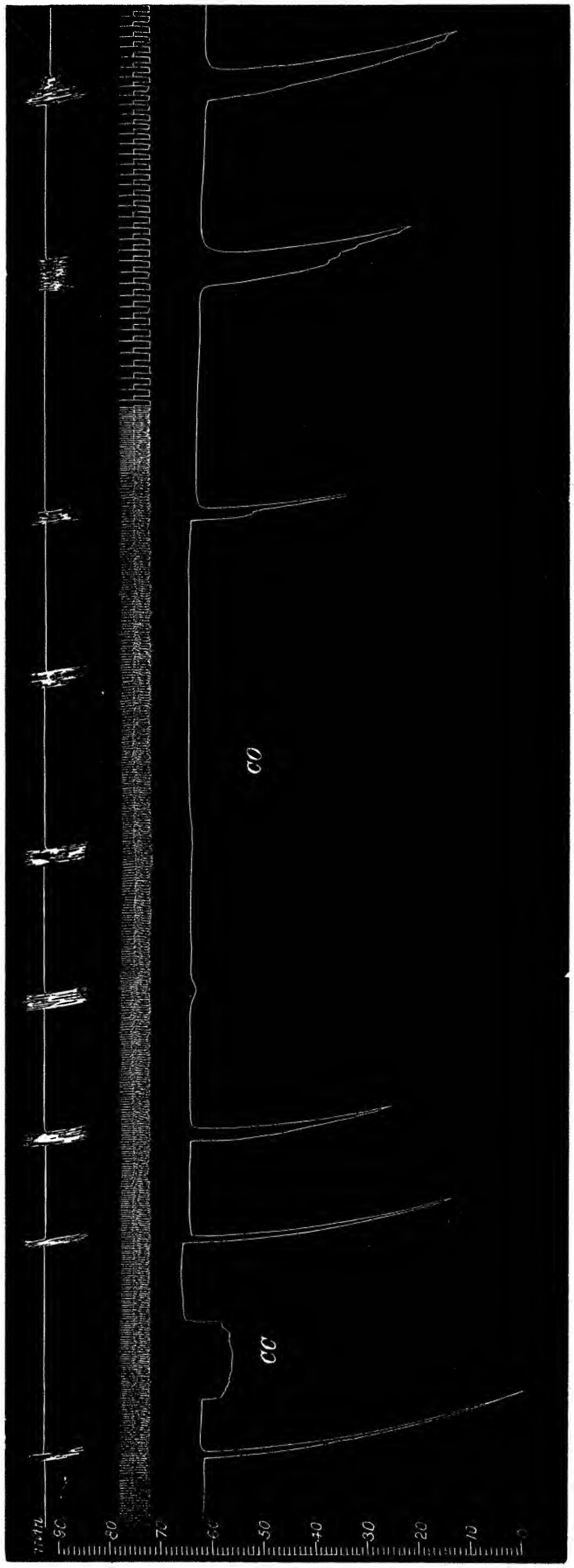
Absinthe (5 minims) is injected intravenously; there results a fit, then extensor spasm and respiratory paralysis. The cortex is excitable during the extensor spasm. On stimulating the arm area the extension is *increased*. The excitability vanished within 1 minute after the failure of respiration.

Note.—The monkey had diarrhœa; the room was very cold, and the brain was not protected with warm wool pads.

VI. *Bonnet Monkey* (*about* 4 *years of age*).

The extensor carpi radialis is connected with an isometric lever, and its contractions recorded. The arm area is exposed, and the carotids prepared. Strength of current just distinctly perceptible to tongue. Contraction of the muscle is obtained by exciting the upper part of the arm area just in front of the fissure of ROLANDO. On clamping the carotids, the brain becomes very anæmic and collapses, and the centre becomes inexcitable. The excitability returns so soon as the clamps are removed.

Fig. 5.—Bonnet Monkey. Ether.



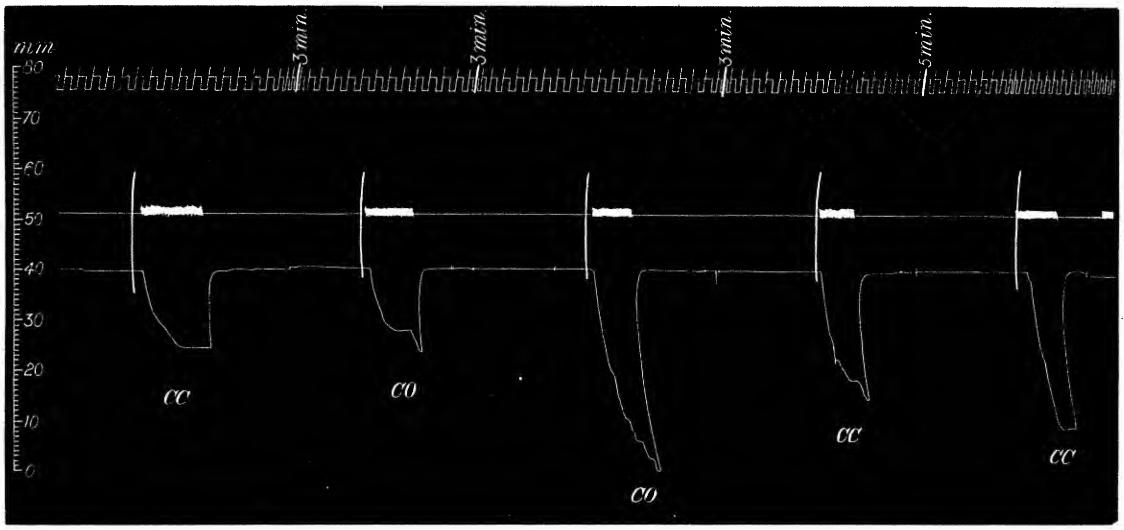
Extensor carpi radialis connected to isometric lever. Cortex excited in arm area just in front of fissure of ROLANDO. CC. Carotids clamped, followed by gradual abolition of excitability. CO. Carotids loosened, followed by gradual return of excitability.

The periods of excitation are marked on the uppermost tracing.

VII. *Young and Vigorous Bonnet Monkey.*

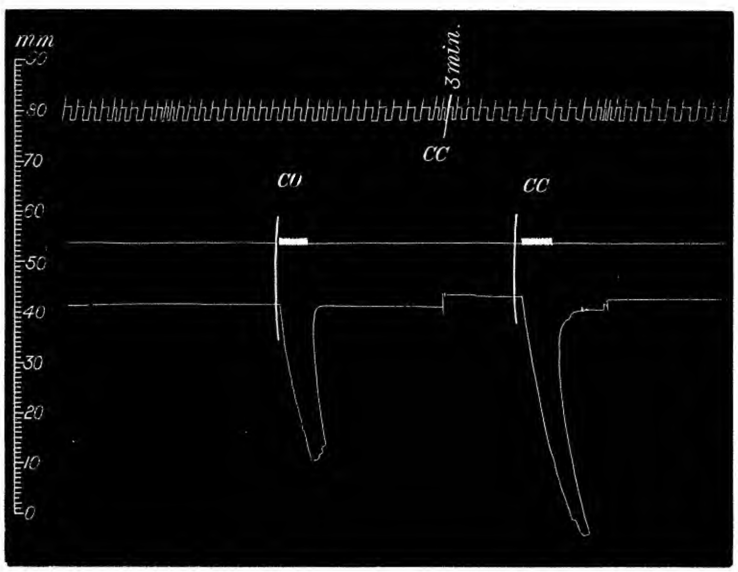
Extensor carpi radialis connected with isometric lever. Carotids prepared; cannula placed in jugular vein; arm area of cortex exposed. Marked contractions are obtained on exciting the upper arm area just in front of the fissure of Rolando. There is no difference in excitability after clamping both carotids, although the brain is exsanguined and collapsed. Excitations, with the carotids clamped or not clamped, are repeated several times.

Fig. 6.—Bonnet Monkey. Ether.



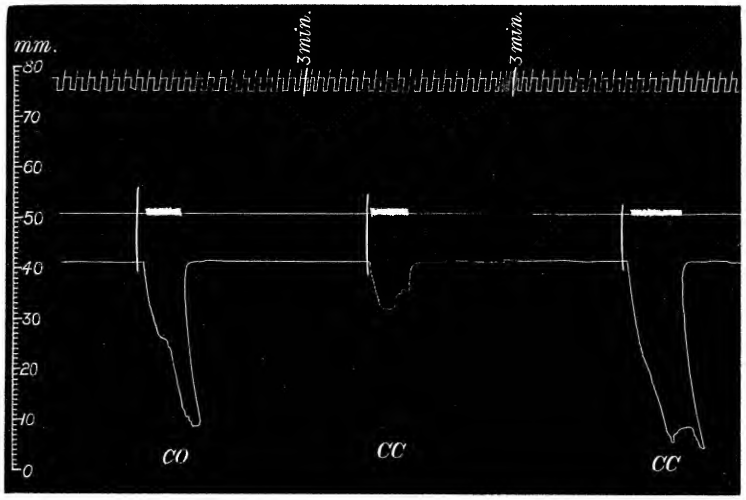
Extensor carpi radialis recorded. Cortex excited in front of Rolandic fissure. CC. With carotids clamped. CO. With carotids loosened.

Fig. 7.—Same Experiment as Fig. 6.



CO. Excitation of cortex with carotids loosened. CC. With carotids clamped.

Fig. 8.—Same Experiment as Figs. 6 and 7.



CO. Excitation of cortex with carotids loosened. CC. With carotids closed.

The carotids are finally clamped and absinthe (3 minims) injected intravenously. There results tonic extensor spasm, while the respiration is deepened and accelerated. On removing the clamps a clonic fit results. The clonus is cut short by reclamping the arteries. On opening the arteries another clonic fit results. (See figs. 10 and 11 in next section.)

These experiments on the dog and monkey render the following points clear :—

1. The cortex cerebri may be markedly excitable when cortical arteries are rendered profoundly anæmic, *e.g.*, by ligation of both carotid and vertebrals in dogs, and ligation of both carotids and one vertebral in monkeys. Fits can often be provoked from the anæmic cortex. It must be noted that the arterial anæmia is often accompanied by venous congestion.

2. The excitability vanishes at once when the anæmia becomes complete.

3. Individual differences are met with in the animals in regard to the amount of arterial obstruction required to abolish the excitability. (Compare Monkeys V. and VI.)

4. The reactions excited from the anæmic cortex are purposive movements, and similar in latent time, &c., to those excited from the normal cortex.

5. The cortex is excitable when the animals are brought into a state of dementia by ligation of the cerebral arteries.

6. Extensor rigidity frequently ensues when the limit of cerebral anæmia is reached, and the excitability is vanishing.

7. Hyper-reflex excitability precedes the development of extensor rigidity.

8. The extensor rigidity is often accompanied by head dyspnœa and spasmodic diaphragmatic respiration, and then general paralysis and death quickly follow.

9. The anæmic respiratory centre can be temporarily relieved by the head-down posture.

In close connection with these experiments stand certain results obtained by MOTT and SHERRINGTON.* These authors determined that, after a unilateral section of all the posterior roots of the brachial plexus has been made in the monkey, the limb is paralysed in so far as no "voluntary movements" occur, such as grasping a raisin. Nevertheless the limb reacted to cortical excitation, and in fact the arm area was, if anything, hyper-excitable. The limb is, we may suppose, paralysed because the spatial sensations which come from the limb no longer stream into the association field formed by the cortex cerebri. The animal forgets that it has the limb. BUBNOFF and HEIDENHAIN† showed that by gently stroking a limb the cortical excitability might be increased in the area which controls the same. On the other hand, MARIQUE and EXNER‡ proved that circumvallation of a cortical area, by severing the association fibres, produces paralysis just as much as extirpation. The "motor centres" are therefore not autonomous, and are only reflexly aroused into activity. It has been suggested that the paralysis following division of the posterior roots is due to lowering of the excitability of the spinal centres (BASTIAN), for these are cut off from the normal reflex excitations. In my experiments there is no question of spinal centres. The cerebral anæmia evidently produces a block on the sensory side, for the animals are demented. There is, moreover, a marked diminution in the turnover of sensations into those appropriate motor reactions, which express the normal condition. Nevertheless the cortex is excitable and even hyper-excitable to electrical excitation. The block, we may suppose, takes place in the weak links of the chain, namely, in the synapses between the afferent axons, the association cells, and the cells which discharge the motor impulses. The large pyramidal cells and their axons which form the pyramidal tract resist for a longer time the deficiency of nutrition. The histological changes are less marked in these cells (MOTT). The interruption of the synapses may unbridle these "motor" cells and render them hyper-excitable, while at the same time it occasions not only paralysis of voluntary movements, but hyper-reflex excitability by blocking the discharge of afferent impulses in the cerebrum. RISIEN RUSSELL§ states that, after a unilateral section has been made of the posterior columns of the spinal cord, the cortex on the opposite side to the lesion discharges movements which are less powerful and more tetanic in nature. It is not easy to bring this result in agreement either with that of MOTT and SHERRINGTON or with my own results. I have noticed that the movements excited from the anæmic cortex are often more convulsive, but not as a rule less powerful. It must be very difficult to divide one posterior column without damaging the adjacent pyramidal tract. RUSSELL's results may be due to the lesion of this tract. The fact that cortical discharge, produced in myself by compression of

* 'Roy. Soc. Proc.,' 1895, p. 484.

† 'Arch. f. d. g. Physiol.,' vol. 26, p. 175, 1881.

‡ 'Arch. f. d. g. Physiol.,' vol. 44, 1889.

§ 'Brit. Med. Journ.,' vol. 2, p. 915, 1896.

the carotid, is unaccompanied by consciousness, is against the theory of BAIN* (supported by WUNDT) "that the sensibility accompanying muscular movement coincides with the outgoing stream of nervous energy and does not, as in the case of pure sensation, result from an influence passing inwards by ingoing or sensory nerves." In this connection we may recall VAN DEEN'S experiment of producing disorder of locomotion in the frog by division of the posterior roots; SHERRINGTON'S experiments, which demonstrate that afferent impulses pass from contracting muscles and inhibit their antagonists;† SHERRINGTON and MOTT'S experiment of producing, in the monkey, by division of all the posterior roots, paralysis of voluntary movement of the hand; and KRAUSE'S observations on the paresis of the face muscles after removal of the Gasserian ganglion in man. These experiments, just as deaf-mutism, show that afferent impulses must constantly stream into the central nervous system during every movement. These afferent impulses, at one and the same time, provoke and co-ordinate movement and enter into consciousness. FERRIER has pointed out that the discharges of cortical, or Jacksonian, epilepsy are not preceded by, or associated with, any sensation further than that which accompanies the muscular contractions.

MOTT and SHERRINGTON, by division of certain roots, found that the tactile sensations from the skin of the hand were of greater importance than the muscular sensations in the performance of voluntary movements. This conclusion is contrary to that drawn by BERNARD from experiments on dogs. In my own case I found that consciousness of the clonic spasms arose from tactile sensations rather than from sensations of movement of the muscles and joints.

SECTION IV.—*The Effect of Absinthe on the Anæmic Brain and the Nature of the Cortical Discharge.*

Historical Review.

The convulsions produced by hæmorrhage or complete anæmia of the brain are similar to those of asphyxia. There first occurs a short lasting tonic contraction of the neck and jaw muscles; then clonic contractions of slow *tempo*, consisting of powerful and general flexor and extensor spasms—these spasms differ widely from the rapid clonus of isolated muscle groups which occurs in the cortical epilepsy of the monkey. There then follow tetanic extensor spasms, long-drawn respiratory gasps, and death.

1. NOTHNAGEL produced similar convulsions in rabbits by stabbing the neural axis with a needle in the region of the pons. These convulsions were, he said, epileptic in type, and were accompanied by loss of consciousness. The latter he ascribed to irritation of the vaso-motor centre, and consequent spasm of the cerebral arteries and

* *Cit.* after FERRIER, 'Funct. of the Brain,' London, 1886.

† "Proc. Physiol. Congress," 'Journ. of Physiol.,' 1898.

anæmia of the cortex. This vaso-motor theory of the loss of consciousness was the natural outcome of KUSSMAUL'S localisation of a convulsive centre in the spinal bulb. This theory has, in my opinion, no basis in fact, for excitation of the vaso-motor centre, by increasing the arterial pressure, accelerates the flow of blood through the brain.*

ALBERTONI, moreover, has shown that complete fits are produced equally well after as before division of the cervical sympathetic nerves.†

The localisation of a convulsive centre in the bulb has been overthrown by the discovery of cortical epilepsy (HITZIG and HUGHLINGS JACKSON). Moreover, convulsive movements may be discharged from the spinal cord after a sub-bulbar section of the same has been made. These convulsions may be excited by asphyxia (LUCHSINGER) and by anæmia (SCHIFF, S. MAYER).

2. SCHÄFER and HORSLEY‡ obtained clonic convulsive movements in one or two cases on exciting the peripheral end of the divided spinal cord.

3. BINSWANGER states that the convulsions produced by stabbing the pons in the rabbit are not true epileptic spasms, but consist of tonic convulsions and movements, such as kicking, stamping, and walking. "Im Boden der Rautengrube," writes BINSWANGER, "liegen in der lateralen Abschnitten von dem medialen Abhängen der clavae bis zum vorderen seitlichen Begrenzungswinkel des Ventrikels reichend, eine Reihe elektrisch und zum Theil mechanisch erregbarer Punkte. Diese antworten auf Reizung mit tonischen Krampf-zuständen des Rumpfes, Kopfes und der Extremitäten ohne locomotorischen Effect. Diese motorischen Reizerscheinungen sind reflectorischer Art. Die Reizstelle bilden die sensiblen Trigeminuswurzeln, vornehmlich die aufsteigenden, vielleicht ist auch eine im seitlichen Felde der Formatio reticularis gelegene sensible Haupt-bahn Vermittlerin des Reizes. Diese Reflexcentren der Brücke besitzen die Bedeutung einer Sammelstation der Niveau-centren des Rückenmarks, sie dienen der Vermittlung umfassender associirter Bewegungen — Es gelingt niemals, weder durch elektrische noch mechanische Reizung, von der Brücke aus wahre epileptische Anfälle auszulösen."§ This is contrary to the views of NOTHNAGEL and HEUBEL.||

4. WYRUBOW, working in BECHTEREW'S laboratory, concludes, in opposition to BINSWANGER, that true epileptic fits are produced in rabbits by the stab of a needle in the pons, and in dogs by electrical excitation of the same part.

5. BECHTEREW¶ believes that these fits are produced by reflex excitation of the cortex cerebri, for after a complete section of the brain has been made at the level of

* *Cf.* 'Cerebral Circulation,' p. 68, 1896.

† 'Ctbltt. Med.,' 1882.

‡ 'Journ. of Physiol.,' vol. 7, p. 96, 1886.

§ 'Die Epilepsie,' p. 30, 1899.

|| 'Arch. f. Path. Anat.,' vol. 4, p. 1, 1868.

¶ 'Neurolog. Ctbltt.,' vol. 14, p. 394, 1895.

the corpora quadrigemina no true fit can be produced, but only "einige zerstreute krampfhafte Zuckungen." BECHTEREW suggests that the cortex is excited by the hyperæmia which follows excitation of the vaso-motor centre. Against this view, which is exactly the opposite to that of NOTHNAGEL, are the experiments which I have related in the last section.

6. BECHTEREW and J. MAYER determined that injection of absinthe, after the neural axis had been divided above the pons, produced only opisthotonos and general tonic extension of the limbs. They conclude that clonus with *quick tempo* can only be excited from the cortex cerebri, and that there is no evidence of a convulsive centre in the pons.

7. BOYCE,* after removal of one cerebral hemisphere in cats, found that absinthe produced bilateral convulsions, but the spasms on the side opposite the lesion were delayed in onset and the clonus was less marked. (The bilateral clonus may well have been discharged from the one hemisphere.) He states that clonic spasms of *slow* rhythm can be discharged from the bulbo-spinal centres—including the cerebellum—and that the spinal cord is itself excited by absinthe.

8. GOTCH and HORSLEY† state that absinthe discharges no true clonus from the spinal cord. Moreover, after removal of the "motor area" on one side, and injecting absinthe, they obtained clonus only on the side contra-lateral to the sound cortex. Tonus occurred on the side opposite the lesion.

9. SEMON and HORSLEY‡ never obtained clonus of the vocal cords on stimulating the spinal bulb, while this was constantly evoked by cortical excitation.

10. ROVIGHI and SANTINI find that after a unilateral destruction of the motor cortex has been carried out, pikrotoxine and cinchonidine produce only tonic spasms on the contra-lateral side.§

Convulsants, such as strychnine, absinthe, santonine, cocaine, picrotoxine, aniline, excite convulsive movements after a sub-bulbar section of the neural axis has been made, but a far larger dose has then to be injected.

11. MAGNAN‖ determined, after dividing the spinal cord, that absinthe in small doses produces only a head fit, while after large doses the legs become slightly convulsed.

Similarly, if the spinal cord of a frog be divided and a small dose of strychnine injected, the arms convulse before the legs (GIRARD). When only small doses of strychnine or picrotoxine are given, the convulsions are altogether arrested by a sub-bulbar section (SCHIFF, HEUBEL).¶ Likewise, after removal of the great

* 'Neurolog. Ctbltt.,' vol. 13, p. 466, 1894.

† 'Phil. Trans.,' B, vol. 182, p. 511, London, 1891.

‡ 'Phil. Trans.,' B, vol. 181, p. 207, London, 1890.

§ 'Ctbltt. Med.,' p. 101, 1883.

‖ 'Arch. de Physiol.,' vol. 5, p. 131, Paris, 1873.

¶ *Cit.* after RICHET, 'Dict. de Physiol.,' vol. 4, p. 408.

brain, the convulsions produced by asphyxia are far less intense in character (Högyes).*

Similarly, ablation of the motor area almost abolishes the convulsions produced by cocaine.†

12. Fr. Franck found that if a cortical motor centre be excised during the discharge of a clonic fit the clonus of the limb supplied by that centre is cut short, and the limb is protected from further clonus.‡ On the other hand, the limb passes into tonic spasm when the current is strengthened. Post-epileptic contracture is not removed by excision of the cortex.

13. Ziehen§ stimulated the subjacent white matter after removal of the cortex of one arm area. He obtained extensor tonus of the opposite arm, while the rest of the body exhibited clonic spasms. On withdrawing the stimulus this arm at once became flaccid, while the clonus of the other parts continued for some little time. Tonus, but no clonus, is to be obtained on cortical excitation of 10-day-old puppies. Clonus, says Albertoni,|| cannot be obtained in rabbits, sheep, or donkeys. It is a characteristic of the higher animals, and especially of the monkey and man.

There is plenty of evidence to show that locomotor and defence movements, and general clonic flexor and extensor spasms of *slow tempo*, can be excited in the lower animals after section of the neural axis above the pons. This is demonstrable in young mammals,¶ but is much more easily shown in frogs. The latter animals are able to leap and crawl so long as the upper third of the spinal bulb is intact (Steiner,** Schrader).††

From the above review, it appears that

1. Convulsions can be discharged from any part of the neural axis, but most easily from the higher parts.
2. Clonus of *quick tempo* is cortical in origin.
3. Tonus is discharged from subcortical centres.
4. Locomotor movements and slow clonic flexor and extensor spasms can be discharged from the spinal bulb, and even from the spinal cord.

Experimental Work.

My experiments with absinthe confirm those of Bechterew and Horsley in a simple but striking manner. Compression of the carotid arteries in monkeys cuts the

* 'Arch. f. exp. Path. u. Pharm.,' vol. 5, p. 96, 1875.

† Richet, 'Dict. Physiol.,' vol. 4, p. 408.

‡ 'Fonct. Motr. du Cerv.,' p. 87 and 88, Paris, 1887.

§ *Cit.* after Binswanger, 'Die Epilepsie,' p. 49, 1899.

|| 'Ctbltt. Med.,' 1882.

¶ Laborde, 'Compt. Rend. Soc. Biol.,' 1887, p. 65.

** 'Physiol. des Froschhirns,' 1884.

†† 'Arch. f. d. g. Physiol.,' vol. 41, p. 75, 1887.

clonic stage out of the absinthe fit, and only tonus results. Similarly, compression either of the four cerebral arteries, or compression of the two carotids after bleeding, has the same result in cats. In dogs the fits are delayed and weakened, but the clonus is not abolished by compression of the four cerebral arteries. This is sometimes, but very rarely, the case in cats.

Cat I.

Demonstration at the Physiological Society, January 20, 1900.

Four cerebral arteries clamped. Three minims essential oil of absinthe (MARTINDALL) injected intravenously. There results extensor tonus of the fore limbs and flexion of the hind limbs. The respiration is deepened and accelerated. On opening the carotids the tonus relaxes, and after a few seconds there occurs a violent clonic-tonic fit. The clonus begins in the neck and face muscles. The fit is cut short, and the tonus returns on recompressing the carotids. The experiment is repeated a second time.

Cat II.

Thirty cub. centims. of blood are withdrawn. The carotid arteries are exposed, and 5 minims absinthe injected intravenously. A violent clonic fit ensues. On compressing the carotids the fit is cut short. Shortly after allowing the blood to flow the clonic spasms recommence. After clamping the carotids and injecting a second dose of absinthe there results extensor rigidity of the fore limbs, while the pupils dilate and become rigid to light. So soon as the carotids are loosened the tonus relaxes, and after a brief interval clonic spasms ensue. After clamping the carotids and administering a third dose the limbs become flaccid and paralysed, and Cheyne-Stokes respiration appears. Asphyxia then produces a few slight movements of flexion and extension, but no convulsions.

Cats III, IV, V.

Repetition of Experiment II., with like results.

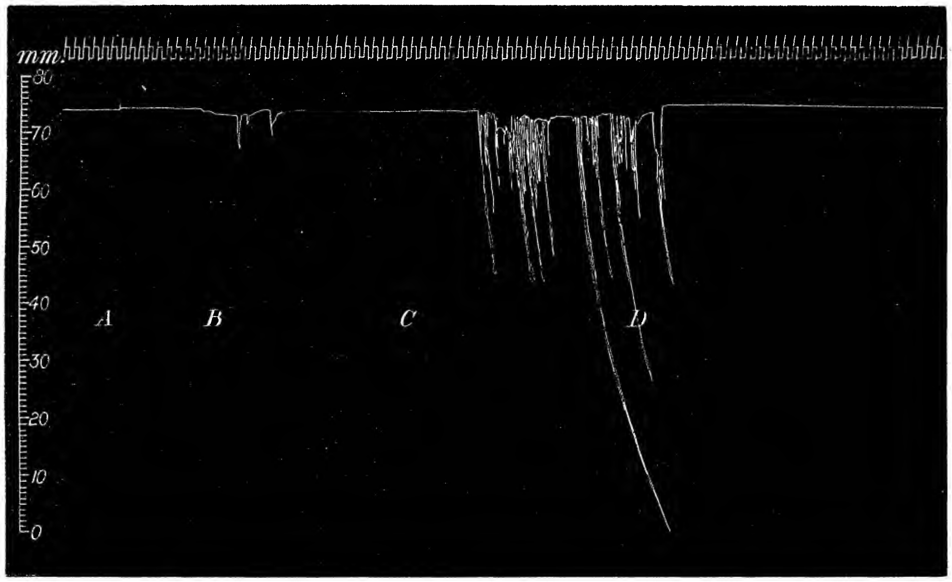
Cat VI.

Four cerebral arteries clamped. Absinthe (3 minims) injected. Slight clonic spasms result. On loosening the carotids there ensues an intense fit, which is cut short by the clamping of the carotids. On opening the clamps the fit recommences. After clamping the carotids and injecting a second dose, extensor rigidity and laboured respiration ensue. The extensor tonus is relaxed on opening the carotids, and a clonic fit follows.

Cats VII and VIII.

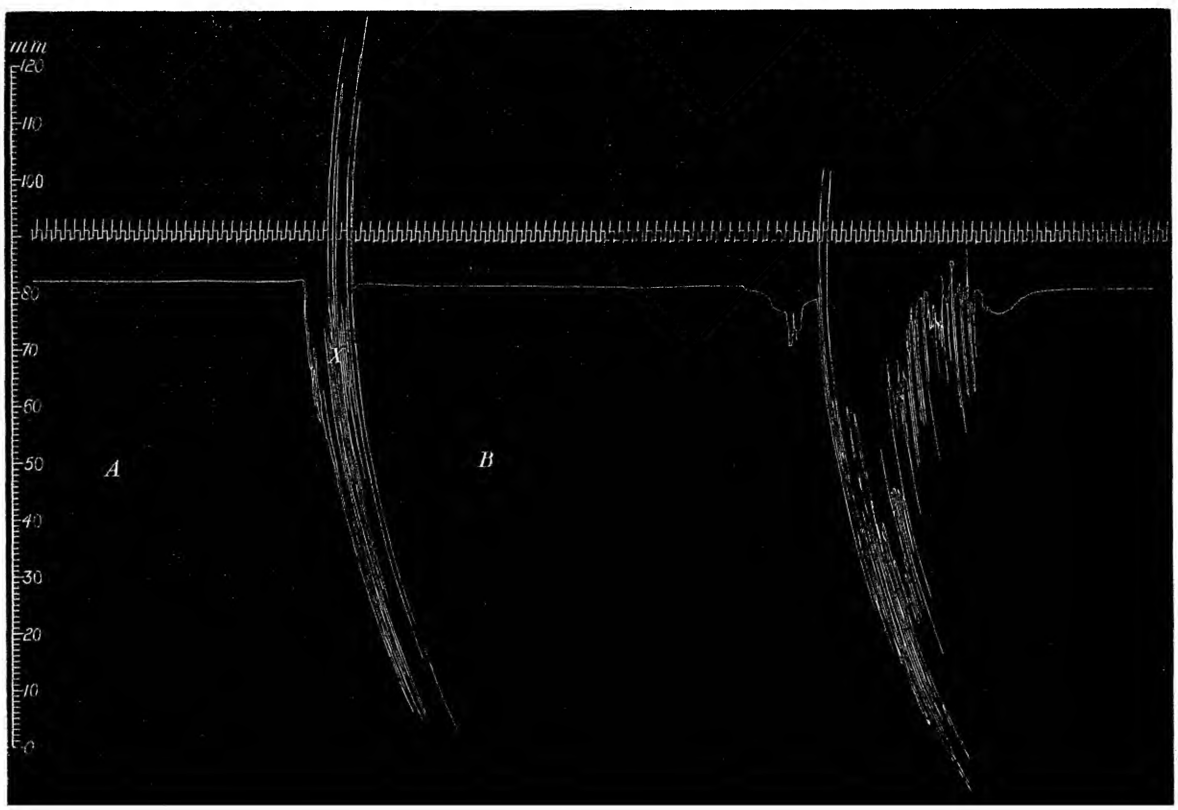
Repetition of Experiment VI. with like result.

Fig. 9.—Cat. Both carotids clamped and both vertebral arteries tied. Flexor communis digitorum recorded.



A. Three minims absinthe injected intravenously. B. Slight convulsive movement. This was followed by extensor spasm. C. Carotids loosened, followed by clonic convulsions. D. Carotids clamped, followed by cessation of clonus.

Fig. 10.—Cat. Ether. Flexor communis digitorum recorded. Both vertebrals tied.



A. Three minims absinthe injected intravenously. X. Carotids clamped, followed by cessation of fit. B. Carotids loosened; after a minute a new fit ensued, and this was allowed to take its course.

Cat IX.

Four cerebral arteries clamped. Contractions of flexor communis digitorum recorded. On injecting 3 minims absinthe, a few slight flexor and extensor movements of the limbs follow, and then extensor tonus of the fore limbs. On opening the carotid clamps there ensue clonic convulsions. The fit is cut short by reclamping the arteries. A second dose is injected after removing the carotid clamps. A powerful fit results. This fit is cut short by clamping the carotids. Soon after loosening the carotids another fit occurs, and this is allowed to take its course.

Dog I.

The four cerebral arteries clamped. Seven minims absinthe injected intravenously. The onset of the fit was considerably delayed. There first occur clonic twitches of the neck muscles, and locomotor movements of the four limbs. Violent general tetanic spasms followed. Removal of the clamps from the carotids causes a momentary relaxation of the tonic spasm. While the tonus continues and the four arteries are clamped, the cortex cerebri is exposed, and the pre-crucial convolution excited. Movements of advancement of the fore limb and drawing up of the hind limb are at once obtained. The strength of current employed is distinctly perceptible to the tongue. The cerebrum is next entirely removed; the extensor tonus not only persists, but is intensified.

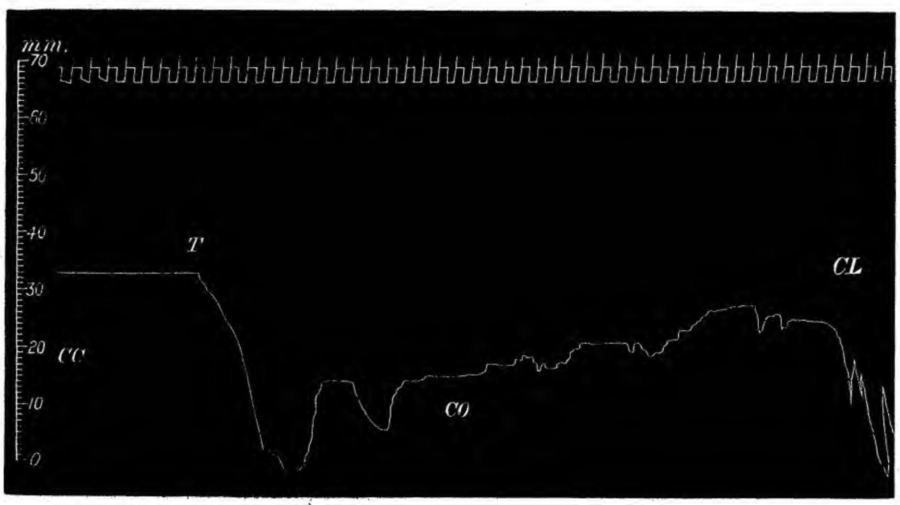
Dog II.

Repetition of Experiment I. with like results.

Bonnet Monkey I.

Carotids clamped. Extensor carpi radialis recorded. 3 minims absinthe injected.

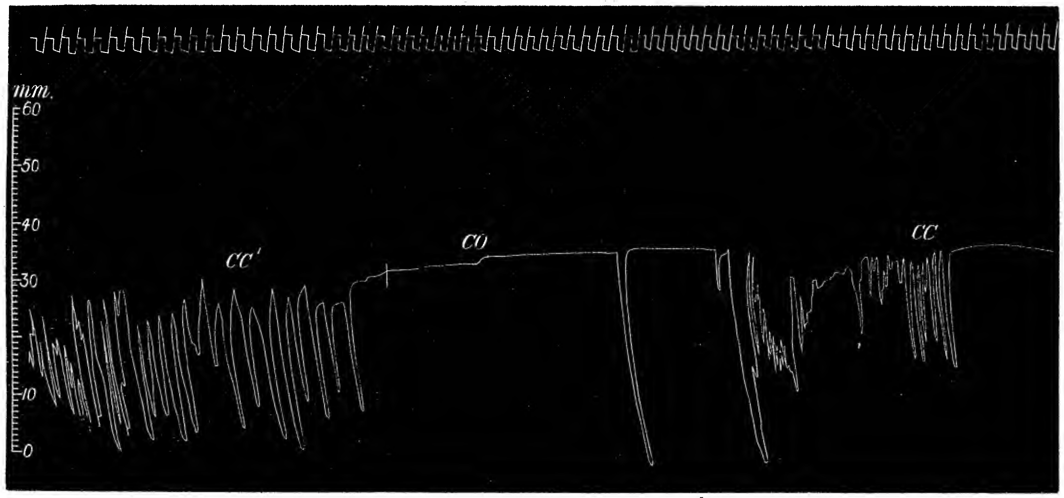
Fig. 11.—Bonnet Monkey. Ether. Extensor carpi radialis recorded.



CC. Carotids clamped and 3 minims absinthe injected intravenously. T. Tonic extensor spasm.
CO. Carotids loosened, relaxation of tonus. CL. Commencement of clonic convulsions.

Extensor tonus and laboured respiration result. On loosening the carotids clonic convulsions ensue. On clamping the carotids the clonus ceases.

Fig. 12.—Continuation of Fig. 11.



CC'. Carotids clamped, followed by cessation of clonus. CO. Carotids loosened, followed by a second clonic fit, and this was also cut short after clamping the carotids at CC.

Rhesus Monkey, II.

Repetition of Experiment I. with like result.

Conclusions.

(1.) From these experiments it is clear that clonus of rapid *tempo* is cut out of absinthe fits when the circulation of the blood through the cortex cerebri is almost entirely stopped.

(2.) The experiments prove how profound becomes the anæmia of the cortex after ligation of the two carotids in monkeys and of the four cerebral arteries in cats, and yet in this condition of intense anæmia the cortex is excitable and even hyper-excitable. In dogs the cerebral circulation, as has been abundantly proved, remains more efficient after ligation of the carotid and both vertebral arteries.

In this connection I quote an analogous experiment of CYON.* Engaged in establishing an artificial circulation through the brain, he wished to test how much blood passed through the brain from the heart when the cerebral arteries were tied. After ligation of the two carotids and one vertebral in a rabbit, he injected atropine into the right heart. The drug produced no effect on the pupil, while excitation of the cervical sympathetic produced the usual dilatation. This experiment demonstrated how deficient the circulation had become.

* 'Arch. f. d. g. Physiol.,' vol. 77, p. 269, Bonn, 1899.

(3.) The experiments also demonstrate that the clonic spasms are produced by the circulation of the absinthe through the cortex cerebri; that when the cortical circulation is checked the poison actually in the cortex becomes rapidly expended (rendered inert by combination with the cortical substance?); and that it takes a few seconds after renewal of the circulation before the poison circulating in the blood affects the cortex and starts the clonus again.

(4.) The tonus is evidently maintained by the circulation of the absinthe through the base of the brain by way of the vertebral arteries.

(5.) The tonus is relaxed by throwing the cortex again into activity.

(6.) Tonus is finally paralysed by increasing the dose of the drug, and then only feeble convulsive movements can be excited by asphyxia.

FRANÇOIS FRANCK states that a cortical fit may be cut short by arrest of the heart or closure of the trachea.

It has on several occasions and at different epochs been demonstrated upon man that compression of the common carotids can cut short or modify epileptiform convulsions.

ALLIEI* stopped by such means the spasms of hydrophobia. STROHELIN† used compression of the carotids with effect on two cases of epilepsy.

REIMER‡ cut short a fit by compressing both carotids in the predromal stage. The case was one of severe and intractable epilepsy. On removing the thumbs from the artery the fit did not return. More recently ROHEIM§ stopped by the same means a unilateral convulsion after all other remedies had failed, and KELLY|| stopped severe eclampsia which had continued for $1\frac{1}{2}$ hours. These are only a few examples taken at random to illustrate the fact that the results obtained on man agree with those obtained by me with absinthe. While sudden compression of the carotid arteries in certain men, such as SCHIFF and myself, may excite the cortex and evoke clonic spasms, the same means, if continued, can be used to paralyse the cortex and cut short an epileptic fit. If, as is probable, certain forms of epileptic convulsions are produced by toxins circulating in the blood, such as carbonate of ammonia (KRAINSKY),¶ then the clonus in such cases ought to be cut short by compression of the carotids and return again on loosening the arteries. The blood of epileptics taken during a fit is said to contain a convulsant, but I have not yet had an opportunity of testing such upon animals.

* 'Med. Chir. Rev.,' vol. 20, p. 265.

† 'Arch. Gén. de Méd.,' March, 1841.

‡ 'Deutsche Klinik,' vol. 8, p. 251, Berlin, 1856.

§ 'Lancet,' vol. 1, p. 45, 1892.

|| 'Lancet,' vol. 2, p. 662, 1892.

¶ 'Allg. Zeitsch. f. Psychiatrie,' vol. 54, p. 612, 1897, and 'Neurolg. Ctbltt.,' vol. 16, p. 697, 1897.

Extensor Rigidity.

1. SHERRINGTON* says: "If transection of the neural axis be carried out at the level of the crura cerebri in, *e.g.*, a cat, there usually ensues after a somewhat variable interval of time a tonic rigidity in certain groups of skeletal muscles, especially in those of the dorsal aspect of the neck and tail and of the extensor muscles of the limbs." This "decerebrate rigidity" is undoubtedly the same as that noted by me in animals in which the cerebral arteries have been tied. When rigidity has been established by a certain degree of anæsthesia, stimulation of the toes, or pad of the feet, or of a flexor motor area, causes, says SHERRINGTON, relaxation of the triceps and contraction of the biceps. In some of my animals I have been able to relax extensor rigidity by rubbing the feet.

2. BUBNOFF and HEIDENHAIN† observed that prolonged tonic spasm occurred in a certain stage of morphia narcosis. These spasms might be evoked either by reflex or cortical excitation. The tonus could often be relaxed by gently stroking the skin or blowing on the eye, or by weak stimulation of the cortex. The tonic contractions seen in hysterical or hypnotised subjects may similarly be inhibited by blowing or stroking the skin.

3. LEWASCHEW‡ having produced a bilateral fit and a condition of tonic contraction on the *same* side as the cortical excitation, was able to relax this tonic spasm by stimulation of the cortex on the opposite side with a suitable strength of current.

RISIEN RUSSELL§ found, after dividing one inferior peduncle of the cerebellum, that absinthe does not excite convulsions of the arm on the same side as the lesion, and the opposite cortical motor area is less excitable. RUSSELL believes that the cerebellum, when unilaterally separated from spinal influences, exerts a greater inhibitory control on the cortex of the opposite side. On the other hand, if one-half of the cerebellum be removed, the restraint of the cerebellum is withdrawn from the opposite cortex cerebri, and then absinthe produces clonic, far more than tonic, spasms on the same side as the lesion.||

HORSLEY and LÖWENTHAL¶ only partially confirm the statement of SHERRINGTON and HERING that by excitation of the cortical area extensor rigidity can be relaxed.

HERING** explains this by saying that relaxation of the antagonists obtains when flexion is provoked, but not when "fixation movement" of the arm is excited from the cortex.

HORSLEY and LÖWENTHAL at the same time determined that excitation of the

* 'Roy. Soc. Proc.,' vol. 60, p. 415, and vol. 62, p. 183, 1897–98.

† 'Arch. f. d. g. Physiol.,' vol. 26, p. 182, 1881.

‡ 'Arch. f. d. g. Physiol.,' vol. 36, p. 282, 1885.

§ 'Brit. Med. Journ.,' vol. 2, p. 915, 1896.

|| R. RUSSELL, 'Roy. Soc. Proc.,' vol. 55, p. 59, 1894.

¶ 'Roy. Soc. Proc.,' vol. 61, p. 20, 1897.

** 'Arch. f. d. g. Physiol.,' 1898.

vermis cerebelli, " most suitably at the line of junction of the vermis superior with the lateral lobe," produces tonus of the triceps and biceps, while on simultaneous excitation of the cortex cerebri and vermis cerebelli a " reinforcement " of the movement is obtained and the clonus is soon overpowered by tonus.

Tonic extensor rigidity is found to be one of the immediate or irritative results of ablation of the cerebellum, while atonicity of the movements of the trunk and extremities is the final result (LUCIANI, THOMAS, RISIEN RUSSELL).

THOMAS* is of opinion that, after unilateral ablation of the cerebellum, the co-ordination of the movements on the same side is no longer automatic, but voluntary, *i.e.*, cortical. The movements have to be relearnt, and are therefore clumsy and inco-ordinate, and become more so on attracting the dog's attention. Tetanic convulsions and rigidity are, according to HUGHLINGS JACKSON and RISIEN RUSSELL, symptoms of cerebellar lesions in man. *In the light of these statements it seems not improbable that extensor rigidity is due to the action of the cerebellum when uncontrolled by the cortex cerebri.* FERRIER is, however, inclined to attribute tonic spasm in cases of cerebellar lesion to the spread of irritation to subjacent parts, such as the corpora quadrigemina, and in agreement with this view is the fact that tonus, evoked in decerebrate frogs by weak stimulation of the skin, is abolished by section of the neural axis below the optic lobes.† In my experiments I have found that the extensor rigidity established by anæmia persists after removal of the cerebral hemispheres, and disappears before the paralysis of the respiratory centre, so that its origin is localised to the cerebellum, pons, and mid-brain. DANILEWSKY‡ has recently determined that tonic spasm may be both evoked and inhibited (by skin stimulations) in the lower limbs of frogs after the spinal cord has been divided for some months. Tonus may therefore be of spinal origin.

SECTION V.—*The more Remote Effects of Ligation of the Cerebral Arteries.*

After extensive destruction of the cerebrum on both sides, GOLTZ noticed the following kind of symptoms: The animals are dull and stupid in behaviour and slow in action, but are able to walk, run, and leap. All four limbs slip outwards on a smooth surface. The legs are often crossed or lifted high like a hen in walking. The animals cannot hold bones with their paws and push them about with their mouths. Circus movements occur to that side on which the cerebrum is more injured. They frequently will stand with one foot on the top of another, or in a basin of cold water, and do not remove a foot placed on a trap-door when the latter is gradually lowered. They stumble downstairs, and on leaping from a table their legs give under them. A clip placed on the foot is neither localised nor removed,

* Article "Co-ordination," RICHET, 'Dict. de Physiol.,' vol. 4, p. 430.

† VERWORN, 'Arch. f. d. g. Physiol.,' vol. 65, p. 63, 1896.

‡ 'Arch. f. d. g. Physiol.,' p. 202, 1899.

although the animals are rendered restless thereby. They often cannot find their food, and may bite the basin, their own feet, or that of another dog instead of a bone. Pieces of food are allowed to drop, or hang out of their mouths. The tongue is never bitten and is freely movable. The animals do not seek their kennels to sleep, or run to the door when the servant is bringing in food. They answer to a call by pricking the ears and wagging the tail. They often run into obstacles, show no fear of a flame, or of the laboratory servant dressed as a guy, and take no notice of a rabbit or of pieces of meat tied under their bellies or suspended above their heads. They reflexly resist interference and growl, and have lost all restraint over the expression of the feelings. If quietly handled they may be placed in the oddest positions. The dogs take no notice of chloroform or tobacco smoke, and will sometimes eat dead dog or a brain which has been hardened in alcohol. The animals empty their bladders and bowels normally, but before doing the latter often run round restlessly in circles.

These symptoms become less marked with time, but in the case of GOLTZ's famous cerebrum-less dog, the animal remained for eighteen months demented, incapable of seeking its food, and behaving as a hyper-excitable reflex machine.

Experiment I.

On December 4, 1895, at 3 P.M., I tied the two carotid and two vertebral arteries in a dog with aseptic precautions. The animal survived and the wound healed by first intention. The condition of this dog, and of others treated in the same way during the next few days, exactly resembled the state described by GOLTZ.

December 5, 10 A.M. The dog alternately sleeps and wanders aimlessly round the room. When asleep several stimulations are required to arouse him. There is a continual tendency to turn to the left. Sleep overtakes him at any moment and in any place during his perambulation. He tries for minutes together to get through impossible crannies and bumps his head into every obstacle in the way, and finally drops asleep in front of such an obstacle. When meat is put in his mouth he resists and then eats it reflexly, but does not notice pieces of meat that drop out or hang between his teeth. He drinks reflexly when his nose is put in a basin of water.

The puplis are dilated but react to light. The optic discs appeared pale, with small arteries and large veins. He takes no notice of a flame held before his face.

The dog reflexly answers to a noise by pricking the ears, but does not come to a call, although he wags his tail. He keeps his head almost on the ground and appears as if smelling his way round the room, but showed no concern at tobacco smoke blown into his face. The tobacco smoke caused reflex licking movements.

A cat was placed on the dog's back, and it showed no concern, although the cat spat with rage. Meat lying on the floor was unnoticed. The mouth temperature

equalled 36° C., while the rectal temperature was 39° C. This showed the deficiency of the circulation in the head. The pulse was 120 and of high tension, the respiration normal. The urine was passed naturally, but without lifting of the leg.

December 6. The animal is in much the same condition. He reacts much more rapidly to sounds. Starts back on the firing of a match and follows the light with his eyes, but shows no fear of the flame or of a hissing and scratching cat. He is stronger on his legs but still turns to the left. Is able with difficulty to pick up and eat meat when this is thrown before him. Is sensitive to a skin-prick.

December 7. The animal is less demented, in so far that he came forward when I entered the room and responded to a call.

December 8. He responds to a call and to patting, and draws the head away from a flame. Cannot localise a clip placed on the ear or toe. Still very sleepy, and goes to sleep in the most extraordinary positions. For example, he can be laid on his back, or stood on his head and propped up against a cage. Quite unable to jump from the smallest height, gazes hesitatingly over the edge. He growls and turns to bite when irritated by pulling out his leg. Howled when meat was placed in his mouth, and then chewed and swallowed it. Rectal temperature, 38·5.

December 9. Very obtuse and soporose. Would neither respond to offers of meat or drink. Was fed with an œsophageal tube. Growls on being interfered with.

December 10. Ate meat when placed in the mouth but refused to lap water. I injected glycerine into the rectum and the dog ran round and round the room many times, then passed fæces and straightway fell asleep on the top of them. Scarcely notices and certainly does not localise a clip placed on the ear or feet. I put a bag over his head and the dog took no notice of this, and made no attempt to take it off. When a string was tied from his tail to a post, he wound himself round and round the post, finally tried to get under his tail, and then fell asleep.

After this date the dog rapidly recovered, and by December 14 the dog was practically normal, save for some weakness of the limbs and hesitation in jumping from heights.

On December 16 the dog was killed, the ligatures verified, and the superior intercostal branches which enter the anterior spinal artery were found to be dilated to the size of the vertebral arteries.

Experiment II.

The second dog, a young fox terrier, after the ligation of the four cerebral arteries recovered without any marked period of dementia. Weakness and straddling of the limbs were noticeable on the first day after the operation and no other symptoms. The animal was kept for a month and then killed and the ligatures verified.

Experiment III.

Dog.

March 23, 1896. All four cerebral arteries were tied within 10 minutes. On coming round from the anæsthetic the animal's limbs gave under him, and he was quite oblivious to a clip on the foot, to a lighted match, or tobacco smoke. The optic discs were pale and the veins about five times the diameter of the arteries. He answered reflexly to a call by wagging his tail. On the third day the animal walked with the legs straddling over a wide base, and clips on the skin were not localised. The dog smelt and ate food which was placed on the floor. On the fourth day I killed the dog with chloroform and injected the aorta with carmine-gelatine. The whole of the base of the brain was injected by way of the superior intercostal and anterior spinal arteries. The injection barely reached the upper surface of the cerebrum or cerebellum; the temporo-sphenoidal lobes were fairly well injected. The other organs of the dog were perfectly injected.

Experiment IV.

Young Fox Terrier.

The two carotids, the right vertebral and the left subclavian, were ligatured in one operation. One hour afterwards the animal was soporose, but responded to excitation. Next day it was comatose, and died after a tonic convulsion.

Experiment V.

Dog.

The four cerebral arteries tied in one operation. After the anæsthesia had passed off there occurred a tonic fit accompanied by vocalisation. There was marked reflex hyper-excitability and tremor of the legs.

Second day. The animal is anæsthetic to a clip, and shows no concern at a flame. There is tremor of the legs and a tonic fit occurred after handling the animal. It smells and eats meat placed on the floor.

Third day. The animal is very sleepy. Anæsthetic to the clip test. The tremor of the legs continues. The head is kept touching the ground as it walks. Placed on a table it walked over the edge. A tonic spasm accompanied by vocalisation occurred on handling the animal.

Fourth day. The dog crosses its legs scissorwise and tumbles over. It stands with one front paw on the top of the hind paw. The tremor of the legs is constant. It is rendered restless by a clip on the paw and turns its head towards the right direction, but does not attempt to remove it. The animal was killed on this day, the ligatures verified, and the arteries injected. The upper surface of the cerebrum remained uninjected.

Experiment VI.

Dog.

Four cerebral arteries tied. The animal was shown to the Physiological Society. The symptoms were very slight. The gait was somewhat unsteady and the limbs spread outwards on a slippery surface. It avoided a flame. It completely recovered.

Experiment VII.

Dog.

In this dog the two carotids, two vertebrals, and one superior intercostal artery were tied, all in the space of 10 minutes. Next day there were marked circus movements. For 5 minutes at a time the dog would turn round in a narrow circle. The limbs were weak and slid outwards on a slippery surface. The dog was not anæsthetic, showed fear at a flame, and erotism in the presence of another dog. The dog completely recovered and was killed on the fourteenth day.

Experiment VIII.

Dog.

The four cerebral arteries tied.

Next day the limbs were weak and straddled on a smooth surface. In jumping the legs gave under him. He let other dogs steal his meat and showed no concern at a flame. He avoids obstacles, comes in answer to a call, and feels a clip on his paw. The optic discs exhibit large veins and very small arteries. The dog was killed and injected with methylene blue at arterial tension. The blue matter barely reached further than the base of the great brain, while the rest of the body was well injected.

Two other similar experiments on dogs are reported in the section on cortical excitability.

Experiment IX.

Cat.

Both carotids and right vertebral tied. Two days later the animal showed weakness of the limbs; the hind leg hung back in walking on the sides opposite to that on which the vertebral had been tied. There was divergent strabismus of left eye, the pupils were dilated, and the left nictitating membrane was half drawn over the eye. There was no anæsthesia or dementia. The animal answered to a call, was frightened at a flame, and found and ate meat.

Experiment X.

Cat.

Both carotids and vertebrals tied. The animal after recovering from the anæsthetic was blind. It restlessly moved about. Reacted to a clip placed on the

feet or ear. Another cat scratched it; it jumped back but showed no recognition. Four hours later the cat was sinking into a comatose condition. It was found dead next morning.

Experiment XI.

Cat.

Two carotids and left vertebral tied. Next day the animal appeared to be in a normal condition. Three days later the right vertebral and superior intercostal arteries were ligatured.

There were no severe symptoms. The left hind leg gave out under the animal. Killed on the fourteenth day.

Experiment XII.

Rhesus Monkey I.

Two carotid arteries and the right vertebral artery ligatured. Wrapped up in wool and placed in cage.

One hour later the monkey had escaped from the wool and was sitting up. It recognised the laboratory servant as an object of alarm and retreated when he approached his hand to the back of the cage. It appeared scarcely affected.

Second day. Next day the laboratory servant said the monkey was at the point of death. I found it to be in a profound stupor and in a condition of extensor rigidity. The pulse and respiration were normal, the pupils reacted to light, and the corneal reflex was easily obtained. When grasped hold of the animal became aroused and made a few ineffectual movements to escape. It took notice neither of a lighted match nor of a loud sound. I kept the monkey wrapped in cotton wool, and spoon fed it on milk and sugar.

Third day. The condition of stupor was the same. The animal was aroused from stupor by changing its posture, and when placed on its back struggled like a brainless frog to regain its posture. The extensor rigidity of the limbs rendered its efforts ineffectual. When a stick was placed in its hand it reflexly grasped it, and hung to it as the stick was raised. The grasp of the toes was also strong. A strong spring clip was unnoticed when placed on its skin in different parts.

The legs are less rigid than the arms and the monkey is able to propel its rigid poker-like body forwards by means of its legs. The arms are crossed over each other, adducted and extended. The tail moves freely. Deglutition is normal when milk is placed in its mouth.

Fourth day. Condition unchanged. No reaction to a lighted match, or a bell rung in its ear, or tobacco smoke held under its nose. Clips on the skin were unnoticed. The pulse and respiration continued strong. By sudden extensions of the legs the monkey propelled itself out of its box of wool on to the floor. I picked it up and

held it erect; at this moment the cat walked into the room and came straight across to the monkey. As it approached, the animal made a hoarse guttural sound of alarm and by spasmodic extension of its legs attempted to escape. When the cat approached a second time the animal reacted in the same way. This cat-reaction was very surprising considering the profound dementia, anæsthesia, and extensor rigidity of the animal. I explain it as a corpora quadrigeminal reflex.

Fifth day. Condition exactly the same. No further reaction on the approach of the cat. The spoon feeding was regularly continued. The animal was in the same state of sopor and rigidity, and was killed by chloroform at the end of this day.

The cerebral hemispheres were very much softened and the veins distended.

Experiment XIII.

Rhesus Monkey.

Both carotids and one vertebral tied. One hour later the animal was in a condition of extensor spasm, and throwing itself about the cage with considerable violence. The respiration failed after these convulsions.

Experiment XIV.

Rhesus Monkey.

Right carotid and vertebral tied. The left pupil at once became the larger, and rapid nystagmus occurred. Next morning the animal, on opening the cage, escaped and climbed up to the roof. It was so agile and alert that it required three men to recapture it.

Three days later the left pupil was still slightly dilated; the left carotid artery was tied. There followed nystagmus and twitchings of the limbs. Ten minutes afterwards the animal flew about the room. Next day he escaped again into the roof of the laboratory, and could not be captured for three days. There were no symptoms, and the animal was killed on the tenth day.

Experiment XV.

Rhesus Monkey.

Right subclavian and two carotids tied. The respiration became deepened and accelerated, and the pupils unequally dilated on tying the second carotid. The animal remained in a condition of coma, and died during the same evening.

Experiment XVI.

Bonnet Monkey.

Right carotid and vertebral tied. The vagus nerve was accidentally included in the ligature. The animal recovered without symptoms. On the third day the other

carotid was ligatured; this artery was noticeably increased in size. The animal, on recovering from the anæsthetic, retreated from my finger and showed its teeth. An hour later the monkey was in a condition of hyper-excitability, picking and snatching at everything, eating wool, knocking about the cage with extensor spasms. Intervals of sopor occurred; these became more and more prolonged. Finally, after several tonic spasms, in which it banged itself against the cage, the animal fell over, and died within two hours of the ligation.

Experiment XVII.

Rhesus Monkey.

Both carotids and one vertebral tied.

On opening the cage one hour afterwards the animal escaped and ran round the room, and was so alert and keen of sight and sound as to defy capture for some time. Six hours later the animal was sitting soporose with its head between its knees, but could be aroused temporarily by strong excitations. Its head then slowly nodded down again into the former position. The sopor deepened into coma with pin-point pupils. Next morning the animal was comatose and exhibited Cheyne-Stokes respiration. It died in the twenty-first hour.

Experiment XVIII.

Bonnet Monkey.

Both carotids ligatured. On tying the second carotid a clonic fit occurred. Next day the monkey was alert as ever.

Five days later one vertebral was tied and the other vertebral compressed. On compressing the second vertebral, convulsive movements occurred, and these were repeated on each compression. The second vertebral was not tied, but, nevertheless, the animal died during the night.

Experiment XIX.

Rhesus Monkey.

Two carotids and right vertebral tied. Immediately after recovery from the anæsthetic the left pupil was double the size of the right. There was slow nystagmus of the eyes. The animal sat nodding in its cage with its head sinking lower and lower, until with a start it would open its eyes and raise its head, and again repeat the performance. It showed no concern at a cat, stick, or flame. The respiration became snoring in the evening, and next morning the animal was dead.

Conclusions.

These experiments, while confirming those of ASTLEY COOPER, show that nearly all dogs recover from the ligation in one operation of both carotid and both vertebral

arteries. There only results a temporary period of dementia, accompanied by anæsthesia and paresis. These symptoms are sometimes exceedingly slight in spite of the enormous diminution of blood supply, *e.g.*, Experiment VII., where one superior intercostal artery was tied in addition to the carotid and vertebral arteries. In only two cases have I seen the quadruple ligation produce coma and death in dogs. Cats, on the other hand, cannot endure the ligation of more than the two carotids and one vertebral artery. If both vertebrals be tied, in place of one, the cats become comatose and die within 24 hours. In monkeys the two carotids may, as a rule, be safely tied, and no symptoms result. When one vertebral is ligatured in addition, there results sopor, and this is followed, as a rule, by extensor rigidity, coma, and death in 24 hours. In the demented monkey which survived the triple ligature the motor paralysis and rigidity were far more profound than in the case of the dog. If the arteries be tied successively at intervals of time, then the two carotids and one vertebral artery may be tied in the cat or monkey (Experiment XIV.), and this without the slighest sign of paralysis or dementia. In Experiment XVI., however, the ligation of the second carotid on the third day produced a fatal result.

The demented condition of the animals after ligation of the cerebral arteries and the absinthe experiments described in Section V. seem to prove that these animals are for the time being in a decerebrate condition. The symptoms not only agree with those described by GOLTZ as occurring after extensive destruction of the hemispheres, but also with the classical effects described as following removal of the cerebrum.

After removal of the cerebral hemispheres, says SCHIFF, a rabbit sits quietly and perfectly balanced. Its limbs, if gently handled, may be put in the oddest positions. If more roughly handled the animal hops forward until its nose comes in contact with the wall, and there it remains perhaps for half an hour. The animals when well fed remain quiet, but when starved are restless, move about, and clean their noses. They react reflexly to noise by twitching the nostrils and pricking the ears; the eyes follow a light. (According to CHRISTIANI, the animals may avoid obstacles.) Decerebrate pigeons, says SCHRADER,* fly from the ground to a perch and balance themselves thereon. They do not feed themselves, and are indifferent to other pigeons. Similarly SCHIFF's decerebrate rabbits may, without any of the pangs of Tantalus, stand before a well-filled food trough and die of starvation. Food is reflexly swallowed when placed on the back of the tongue, but the animals satisfy their need by constraint and without pleasure or appetite. "True ascetics," says SCHIFF, "are just as brainless." In my animals, just as after removal of the cerebrum, all those reflexes fail, which do not depend immediately on lower sense stimuli, but on an association of this stimulus with others received from the higher senses. The spatial sensations—the "Lage-, Tast-, und Bewegungs-Vorstellungen"—of MUNK, depending on the sensory nerves of the skin, joints, and muscles, can no longer be brought in unison

* 'Arch. f. d. g. Physiol.,' vol. 44, p. 175

with the spatial sensations and memories which are derived from vision and audition, and "Seelenblindheit und Taubheit" result. Each voluntary action is a reflex which proceeds from the primary association of the mental images of the actual condition of the body, evoked by the sensations of the present, with those other ideal conditions, which depend on the memories of past sensations.

The demented animals, no longer controlled by these associations, resist the application of colocynth to the tongue no more on the third than on the first occasion. Their eyes reflexly follow a light, but nevertheless the animals stumble into obstacles. After severe blows and falls the animals do not know any better how to avoid such in the future. A decerebrate duck, says RICHET, cannot get out of a corner, and this is the most noticeable symptom. The lower the animal in the scale, the less severe are the results of removing the cerebrum. Decerebrate frogs, says SCHRADER, move spontaneously, catch flies, and bury themselves in the earth at the approach of winter. In the higher animals the common reflex defence movements are alone retained, and in my demented monkey the paralysis was most complete. *My experimental results described above, coupled with those on the excitability of the anæmic cortex, confirm the view that motor paralysis produced by the removal of the "motor" area is not due to the loss of an autonomous centre of volition, but is occasioned by the interruption of the connection between the "motor" area and the sensations which stream through the afferent and association pathways of the great brain.*

The experiments also confirm my previous conclusions as to the rate of metabolism in the brain. By a series of experiments NABARRO and I* reached the conclusion that the exchange of gases is far less in the blood that passes through the brain than in that which circulates through the muscles. This is contrary to the conclusions of Mosso,† who, as the result of thermometric measurements, reached the opinion that the brain is often hotter than either the blood or the rectum, and therefore is the seat of active combustion. Mosso, in my opinion, failed both to obtain the true blood temperature and to recognise and eliminate the thermometric effects which follow any change in the relative distribution of the blood in the brain and body. The methods employed by Mosso to excite cerebral activity must have had an enormous effect on the cerebral circulation and on the relative distribution of the blood. Considering that two of the cerebral arteries may be ligatured in the monkey, and three, or even in some cases four, of these arteries in the dog without producing the slightest sign of dementia, it is clear that the brain is not the seat of active combustion. Moreover, seeing that the dogs fully recover, after three or four days, from the dementia, which is usually occasioned by the ligation of the four arteries, it is obvious that the cortex can for hours be kept from death by the merest dribble of blood, aided perhaps by the cerebro-spinal fluid which may percolate

* 'Journ. of Physiol.,' vol. 18, p. 334, 1895.

† 'Roy. Soc. Proc.,' 1892, and 'Die Temperatur des Gehirns,' Leipzig, 1894.

upwards from the base of the brain. Nevertheless, *total* deprivation of blood immediately paralyses the brain.

One fact which has become clear to me is that the degree of anæmia required to produce dementia in the monkey is separated by the narrowest line from that which produces coma and paralysis of the respiratory centre. In only one monkey have I been able to obtain the stage of dementia. In the other animals there have followed either no symptoms or death in a few hours.

The experiments, lastly, seem to prove that the anæmic theory of sleep is insufficient. The brain no doubt becomes more congested with venous blood, and the arterial pressure falls; but I have determined by sphygmometer records* that the fall of pressure is not greater during sleep than during mental work in the recumbent position. In recumbency, with complete muscular relaxation and shallow respiration, the blood congests on the venous side, the heart decreases in rate, and the circulation is rendered more sluggish; but these changes do not in themselves produce sleep. Ligation of two cerebral arteries in the monkey most assuredly produces a greater diminution in the cerebral blood supply, and yet the animal may, after this operation, be most alert and active. To produce sopor in animals, the cortical circulation must be reduced almost to the vanishing point, and to a far greater degree than ever occurs in sleep. The venous congestion, brought about by recumbency, may, and probably does, promote the onset of sleep; but with this there must occur a withdrawal of all sensory stimuli which enter into consciousness, while the resistance in the synapses of the association cells is probably increased by fatigue.

The conclusions drawn from the experiments described in this paper will be found at the end of each section. The histological side of this research is dealt with by Dr. Mott in his Croonian Lectures, 1900.

Dr. Mott has determined by microscopical examination of the anæmic brains by Nissl's method that—

1. The cortical cells in the brains of the demented animals are swollen and diffusely stained. The stichochrome granules are absent, the nuclei are swollen. The veins are congested, and there may occur hæmorrhages in the cortex.
2. The large pyramidal (motor) cells are least affected.
3. The changes occur very rapidly after ligation of the cerebral arteries, and disappear synchronously with the recovery of the animals from the stage of dementia.

In the case of the demented monkey (Sect. VI., Exp. XII.), the cerebrum was softened in patches, many of the cortical cells were degenerated, and there were signs of active phagocytosis. No changes in the neurons were displayed by Golgi's method.

I am greatly indebted to my friend Dr. F. Mott, F.R.S., who has criticised my work, and advised me throughout the course of this inquiry. The expenses of this research have been met by grants from the Royal Society Government Grant.

* 'Brit. Med. Journ.,' 1897.